

DNA Mixture Interpretation Principles: Observations from a NIST Scientific Foundation Review
AAFS 2019 Workshop #10 (February 18, 2019; Baltimore, MD)

Measurement & Interpretation of DNA Mixtures: Performance Assessment Methods

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DISCLAIMER

Viewpoints expressed are those of the presenter and are not intended to reflect the viewpoints of anyone else at NIST (except perhaps Steve Lund and a few friends 😊)

The discussion is based on what makes sense to us and no claim is made that these are new perspectives

ACKNOWLEDGEMENTS

- Sheila Willis
- John M. Butler
- Melissa K. Taylor
- Rich Press
- Peter M. Vallone
- Steve Lund
- All the members of the NIST DNA Scientific Foundation Review Resource Group

DNA: MEASUREMENT & INTERPRETATION

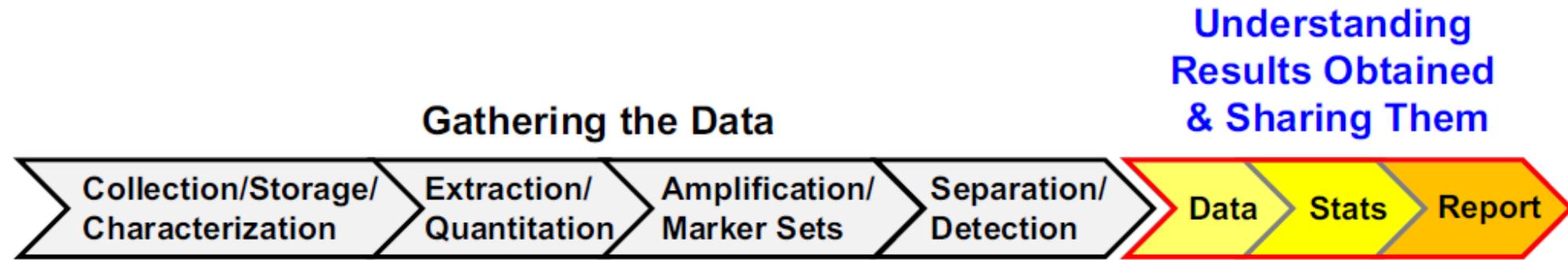


FIGURE 1.1 Steps involved in the overall process of forensic DNA typing. This book focuses on understanding the data through data interpretation and statistical interpretation.

JOHN M. BUTLER

National Institute of Standards and Technology
Gaithersburg, Maryland, USA

Advanced Topics in Forensic DNA Typing: Interpretation

<http://dx.doi.org/10.1016/B978-0-12-405213-0.00001-4>

DNA: MEASUREMENT & INTERPRETATION

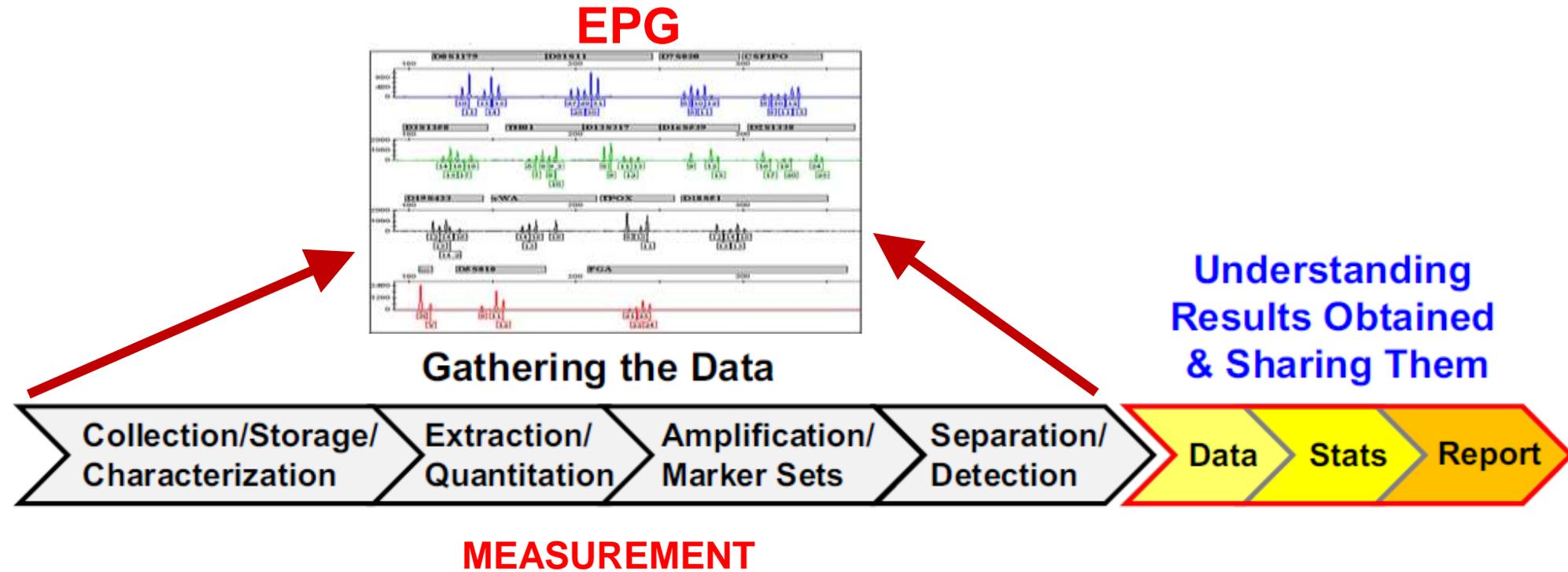


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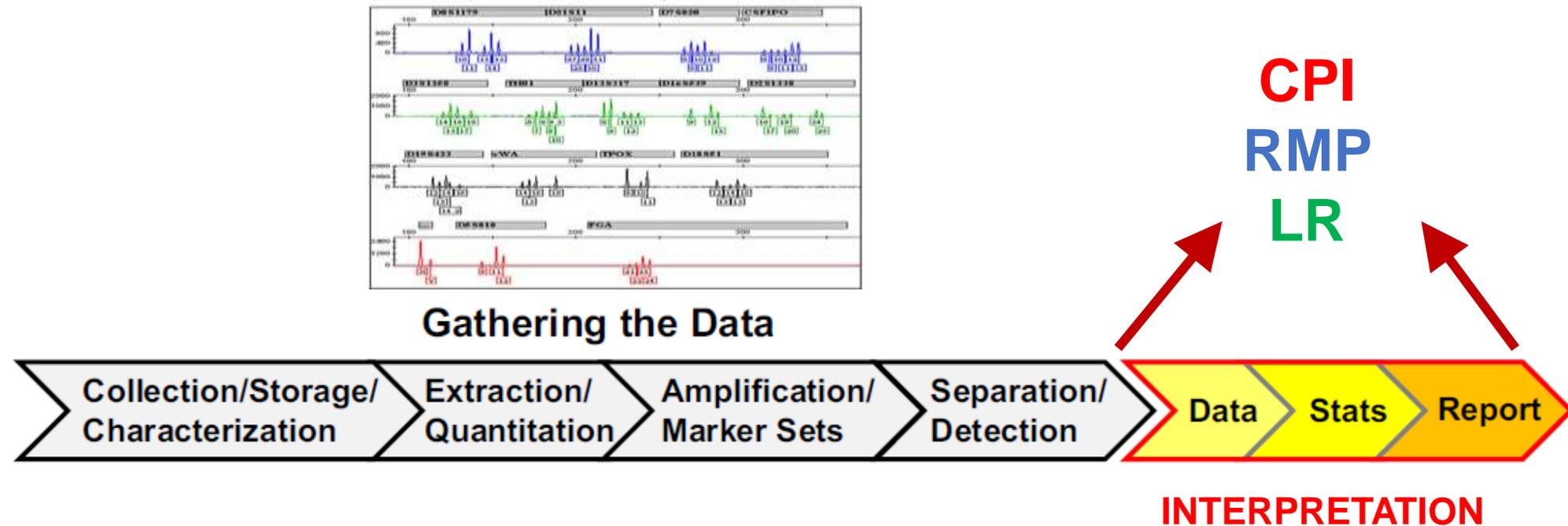
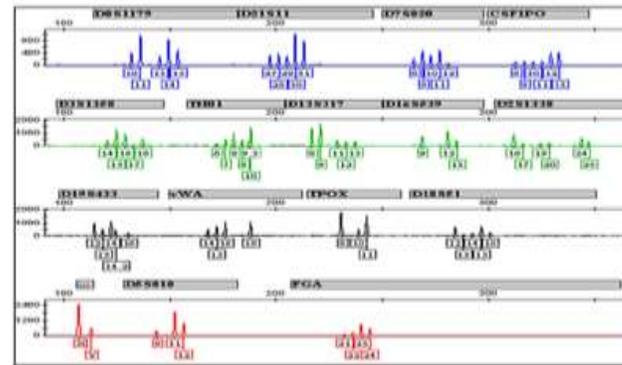


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DNA: MEASUREMENT & INTERPRETATION



LR

Gathering the Data



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LIKELIHOOD RATIO

H_p : DNA from POI is in the sample

H_d : DNA from POI is not in the sample

E = Expert Findings

I = Background Information prior to examining crime sample

$$LR = \frac{Pr(E|H_p, I)}{Pr(E|H_d, I)}$$

DNA: MEASUREMENT & INTERPRETATION

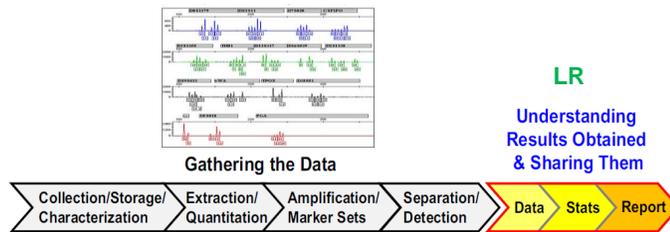
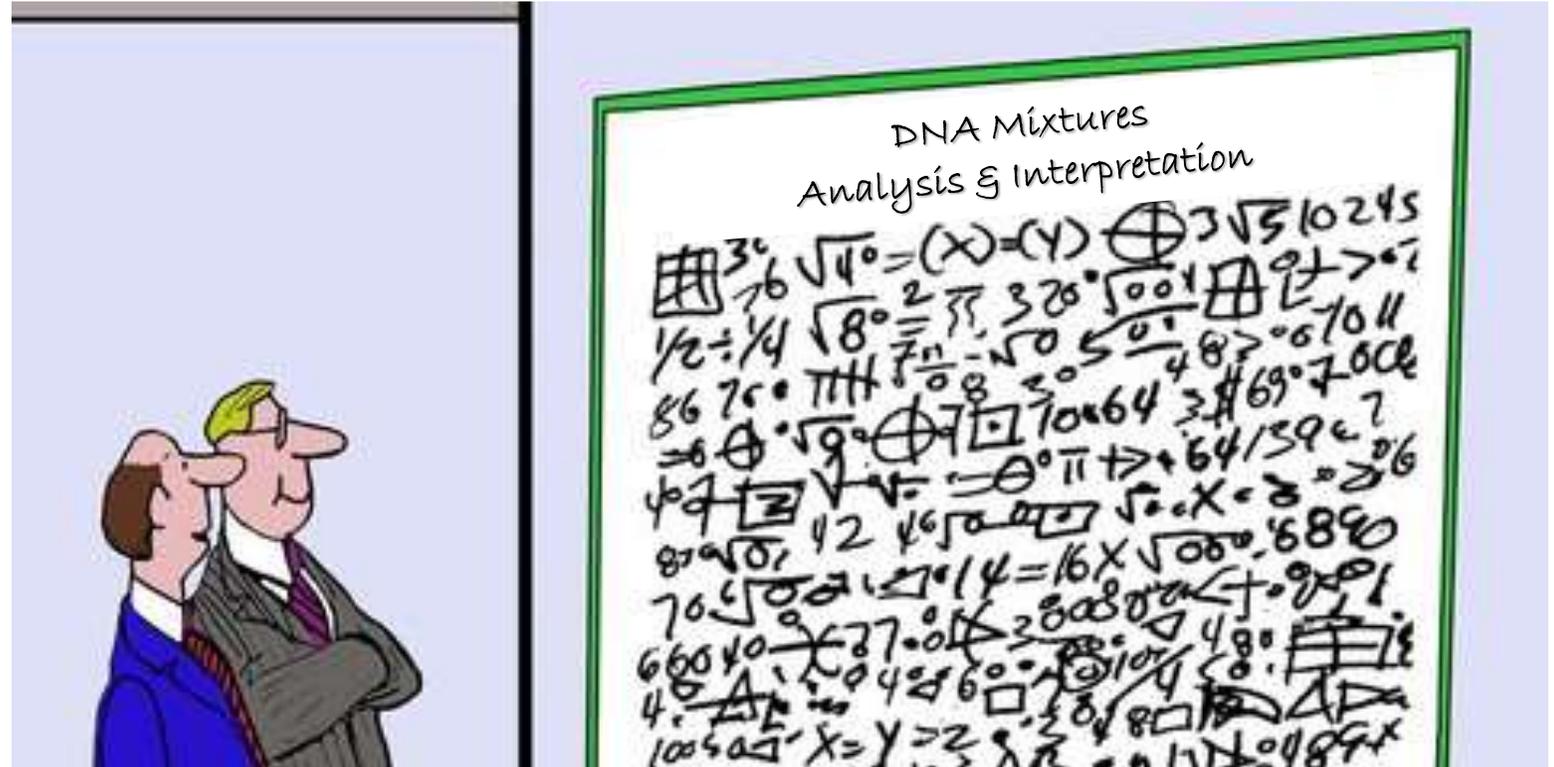


FIGURE 1.1 Steps involved in the overall process of forensic DNA typing. This book focuses on understanding the data through data interpretation and statistical interpretation.

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RELIABILITY

HOW RELIABLE ARE THE RESULTS?

Reliability

The Cambridge Dictionary describes “Reliability” as “how **accurate** or able to be **trusted** someone or something is considered to be.”

reliability

noun [U] • UK  /rɪˌlaɪəˈbɪləti/ US 

[<https://dictionary.cambridge.org/us/dictionary/english/reliability>]

★ how accurate or able to be trusted someone or something is considered to be:

Competence and reliability are prerequisites for any job.

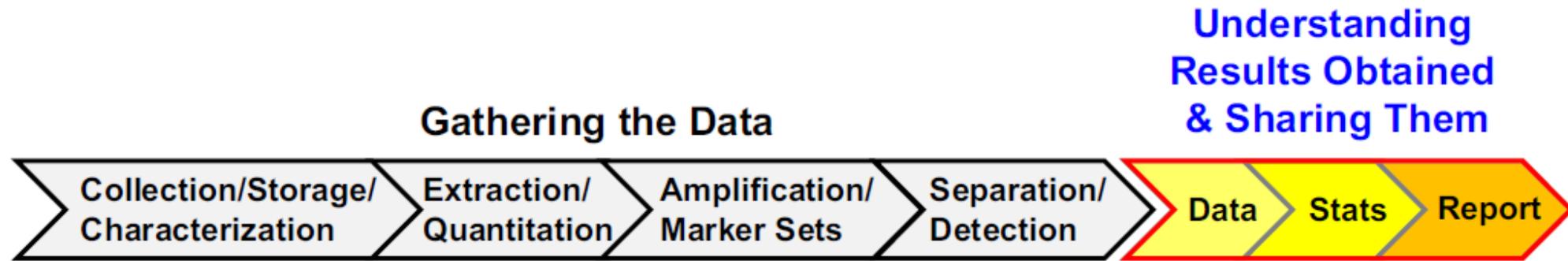
Public confidence in the reliability of a company's financial statements depends on investors perceiving the company's auditors as being independent from the company.

reliability of information/data We have made significant improvements in the reliability of the information held on our database.

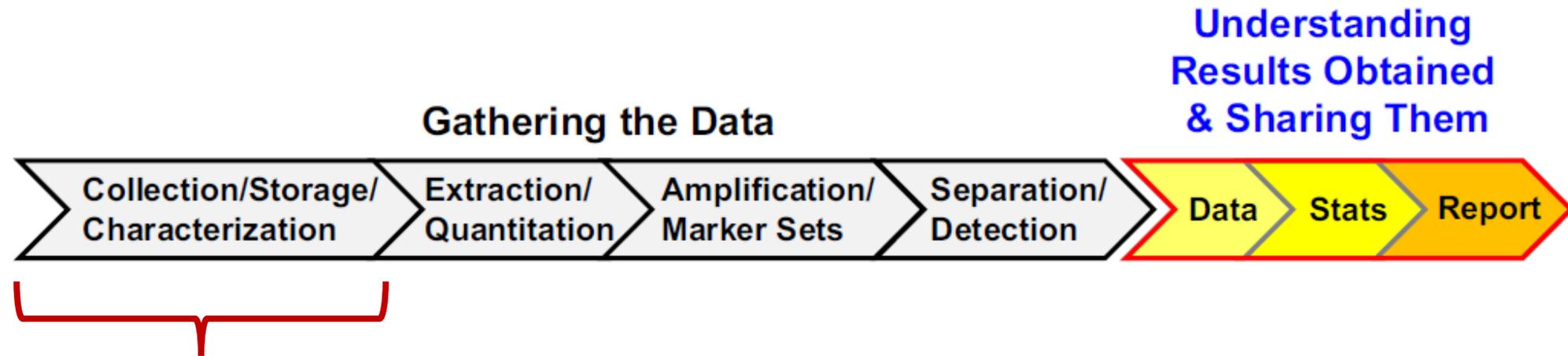
Reliability

- Accuracy
- Precision
- Repeatability
- Reproducibility
- Uncertainty
- Error

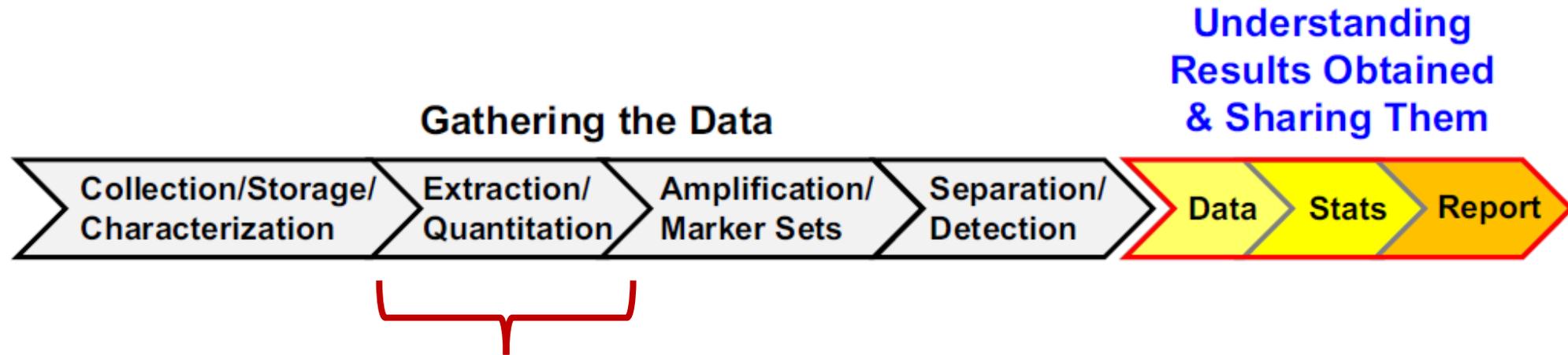
System Reliability vs Component Reliability



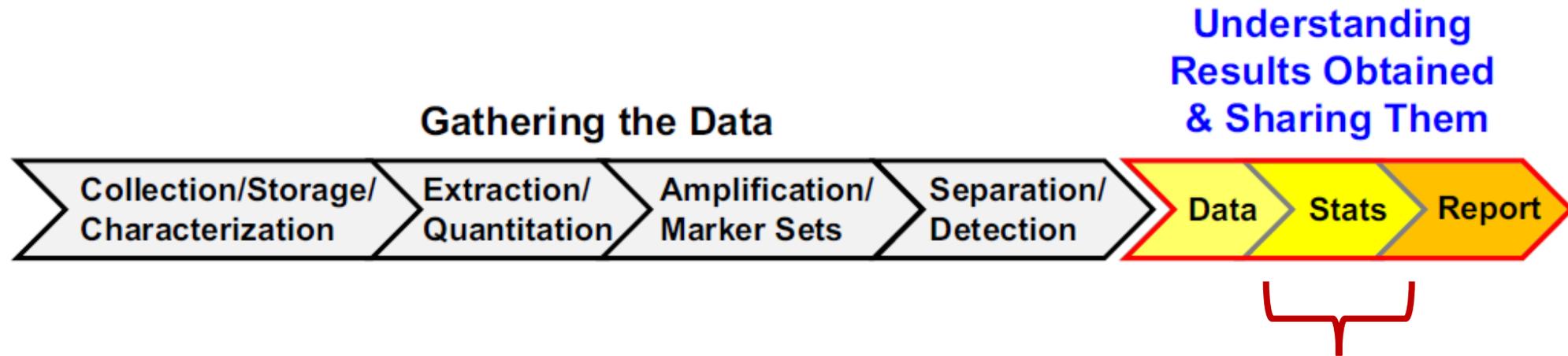
System Reliability vs Component Reliability



System Reliability vs Component Reliability



System Reliability vs Component Reliability



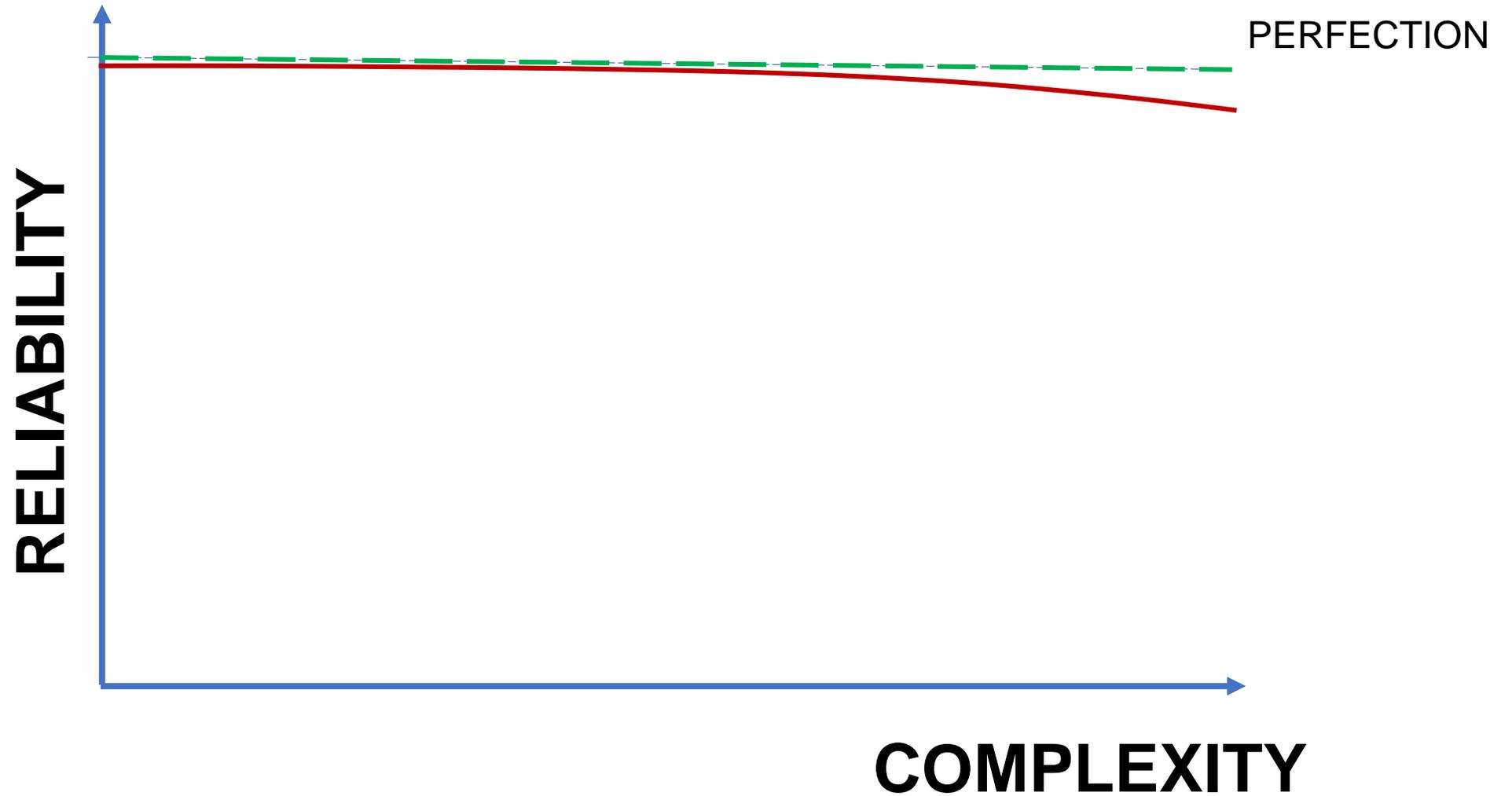
Some Factors Affecting Reliability of an LR System

1. Sample
 - a) Sample amount (contributor template amounts)
 - b) Sample quality (degradation level)
2. Labs
 - a) Kits used
 - b) Equipment Used
 - c) Number of PCR cycles
 - d) Analyst
 - e) Choice of Analytical Threshold (AT)
3. Probabilistic Genotyping (PG) Model
 - a) Choice of laboratory specific parameters for use in the PG model
4. Software Implementing the PG Model
 - a) Choice of numerical methods for computing LR (MCMC, Numerical Integration)
 - b) Choice of burn-in cycles and number of 'accepts'
OR numerical integration parameters (such as grid size)

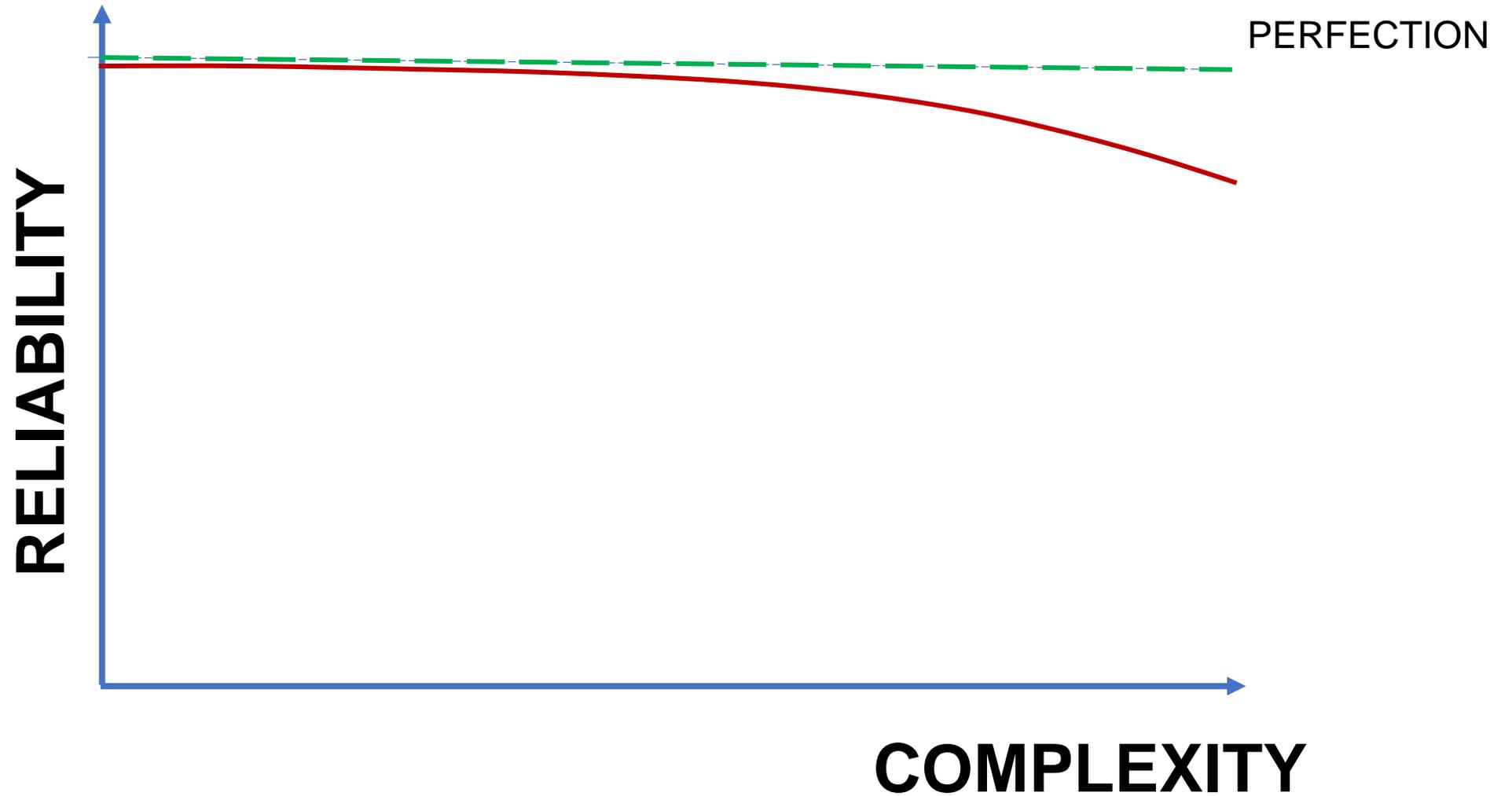
**FACTOR
SPACE**

RELIABILITY vs COMPLEXITY

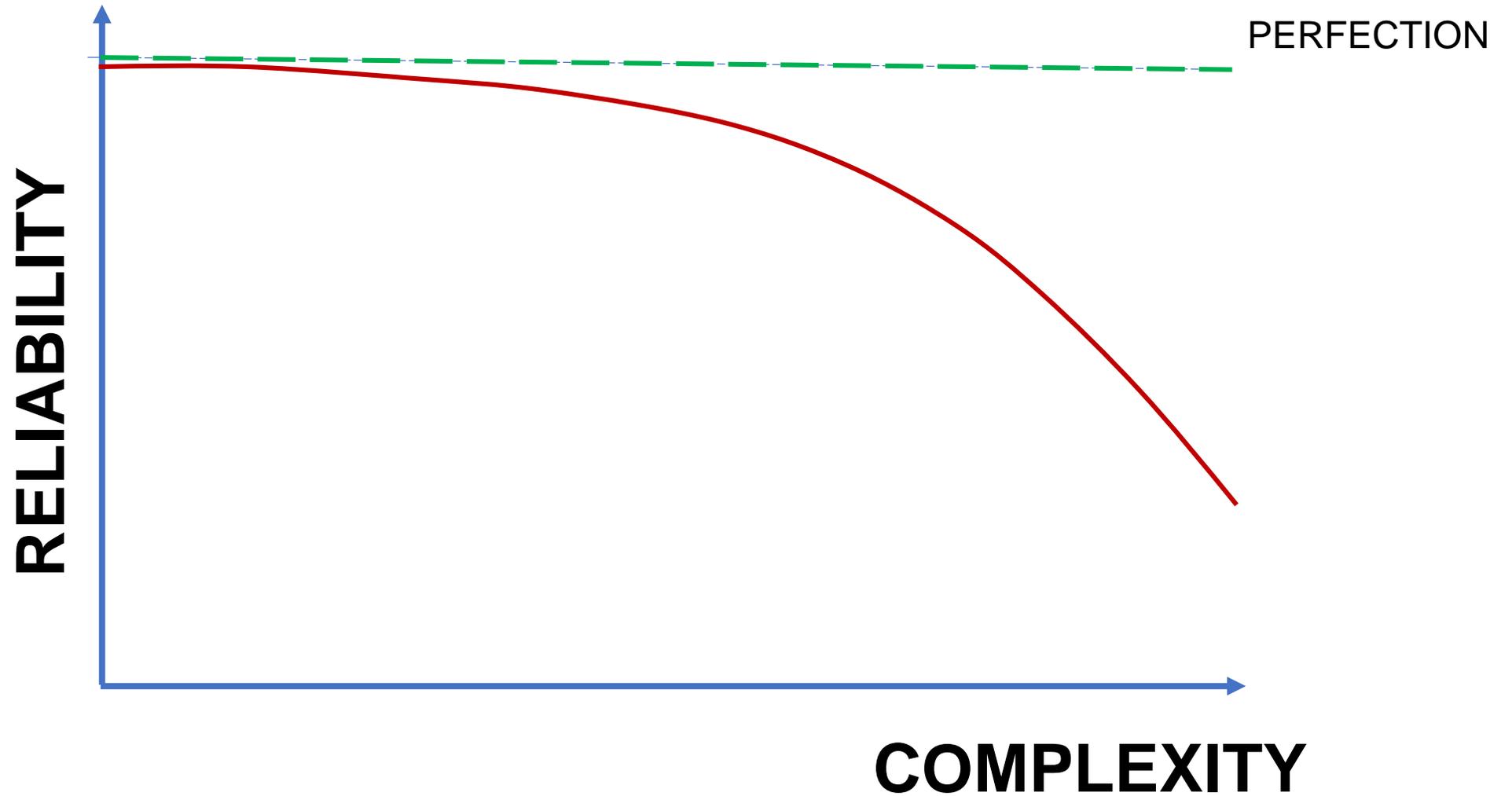
RELIABILITY vs COMPLEXITY



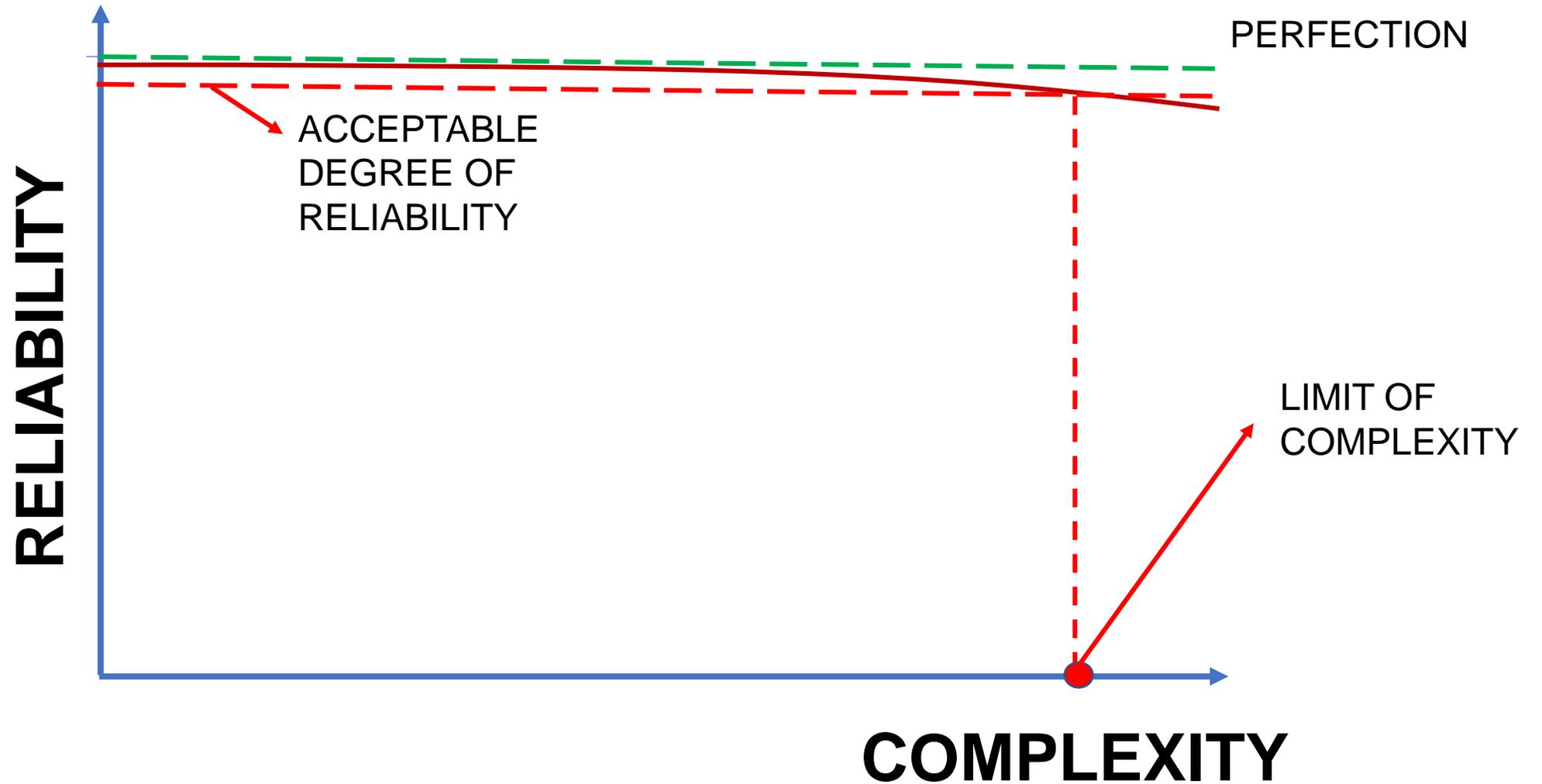
RELIABILITY vs COMPLEXITY



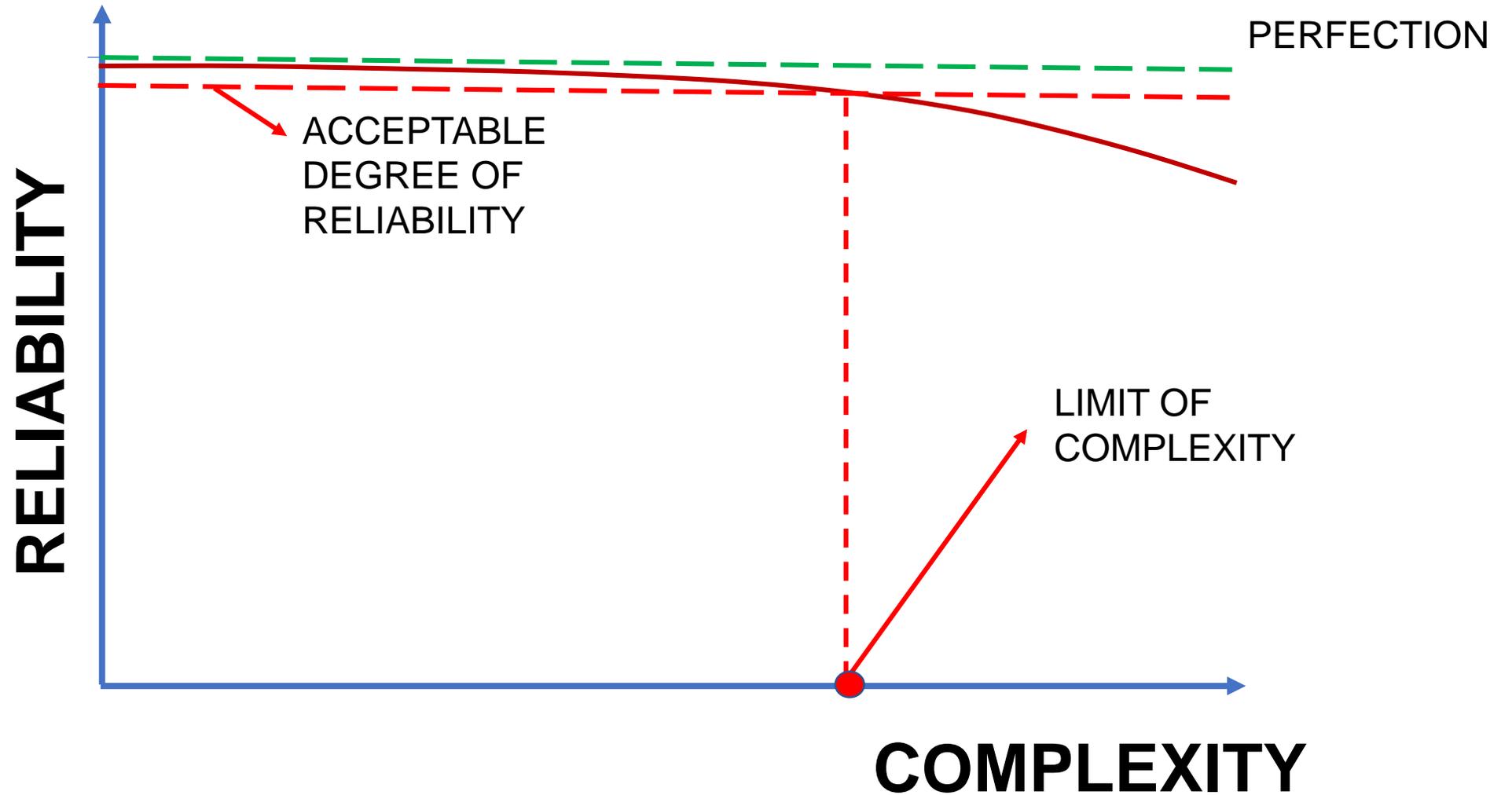
RELIABILITY vs COMPLEXITY



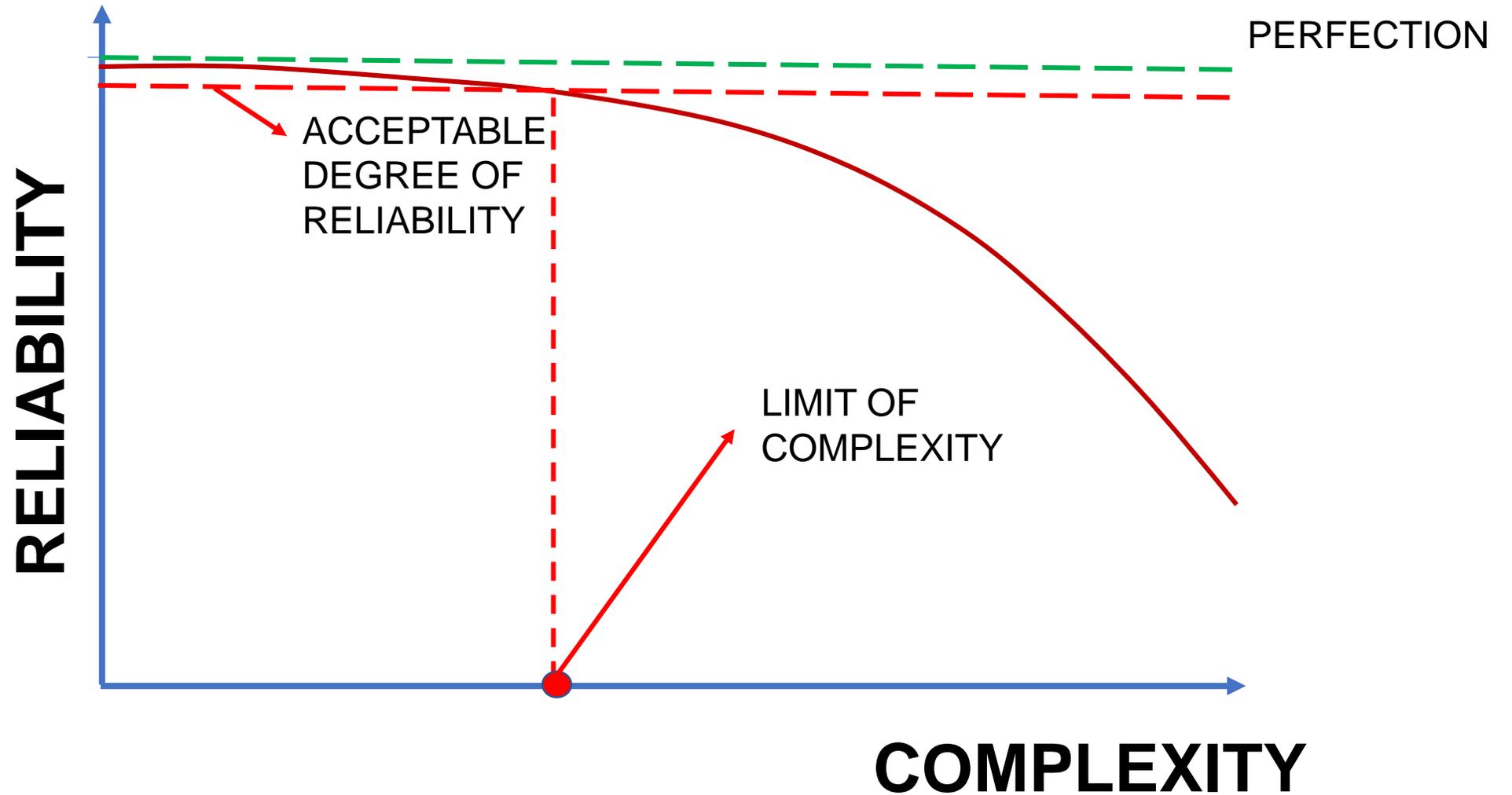
RELIABILITY vs COMPLEXITY



RELIABILITY vs COMPLEXITY



RELIABILITY vs COMPLEXITY



WHY DISCUSS RELIABILITY?

- NAS Report
- PCAST Report

WHY DISCUSS RELIABILITY?

Suppose we send portions of a DNA mixture sample to different DNA labs along with the profile of the defendant in this case.

Will the lab results be close enough to one another that differences between them would be inconsequential to the outcome of this case?

Will the lab results be close enough to the 'true value' that differences between the reported values and the true value would be inconsequential to the outcome of this case?

WHY DISCUSS RELIABILITY?

Cholesterol measurement of 5 aliquots of a sample of blood from 5 labs

148 mg/dl, 175 mg/dl, 215 mg/dl,

375 mg/dl, 450 mg/dl

WHY DISCUSS RELIABILITY?



WHY DISCUSS RELIABILITY?

Cholesterol measurement of 5 aliquots of a sample of blood from 5 labs

146 mg/dl, 151 mg/dl, 162 mg/dl,

155 mg/dl, 166 mg/dl

WHY DISCUSS RELIABILITY?

Cholesterol measurement of 5 aliquots of a sample of blood from 5 labs

146 mg/dl, 151 mg/dl, 162 mg/dl,

155 mg/dl, 166 mg/dl

WHAT IS THE TRUE VALUE?



National Institute of Standards & Technology

Certificate of Analysis

Standard Reference Material[®] 911c

Cholesterol

Certified Cholesterol Mass Fraction: 99.2 % ± 0.4 %

This Standard Reference Material (SRM) is certified as a chemical of known purity. It is intended primarily for use in the calibration and standardization of procedures for the determination of cholesterol in research samples and for routine evaluations of daily working standards used in these procedures. A unit of SRM 911c consists of 2 g of material.

Certified Value: A NIST certified value is a value for which NIST has the highest confidence in its accuracy in that all known or suspected sources of bias have been investigated or taken into account [1]. This certified value is the equally weighted mean of results obtained from the analytical methods. The expanded uncertainty in the certified concentration is calculated as $U = ku_c$. The quantity u_c is the combined standard uncertainty calculated based on a Bayesian approach in reference 1 and the ISO/JCGM Guide [2]. The coverage factor, $k = 2$, represents an approximate 95 % level of confidence. The measurand is the total mass fraction of cholesterol. Metrological traceability to the SI derived unit for mass fraction (expressed as percent).

Details	
Description:	Cholesterol
Lot:	N/A
Expiration Date:	12/31/2024
Unit Price * :	\$814.00
Unit of Issue:	2 g

WHY DISCUSS RELIABILITY?

Cholesterol measurement of 5 aliquots of a sample of blood from 5 labs

146 mg/dl, 151 mg/dl, 162 mg/dl,

155 mg/dl, 166 mg/dl

REFERENCE VALUE = 100 mg/dl !!

WHY DISCUSS RELIABILITY?

Cholesterol measurement of 5 aliquots of a sample of blood from 5 labs

146 mg/dl, 151 mg/dl, 162 mg/dl,

155 mg/dl, 166 mg/dl

REFERENCE VALUE = 100 mg/dl !!

DEVIATIONS: 46, 51, 62, 55, 66

WHY DISCUSS RELIABILITY?

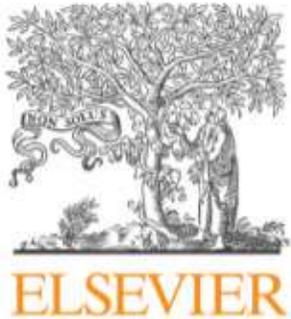
Degree of agreement among a group of labs by itself does not characterize degree of reliability

but

Degree of agreement with respect to a true value or a highly trusted reference value, on a consistent basis, is what characterizes reliability

WHY DISCUSS RELIABILITY?

Forensic Science International: Genetics 35 (2018) 156–163



Contents lists available at [ScienceDirect](#)

Forensic Science International: Genetics

journal homepage: www.elsevier.com/locate/fsigen



Research paper

GHEP-ISFG collaborative exercise on mixture profiles (GHEP-MIX06). Reporting conclusions: Results and evaluation



P.A. Barrio^{a,b,c}, M. Crespillo^{a,c,*}, J.A. Luque^{a,c}, M. Aler^d, C. Baeza-Richer^e, L. Baldassarri^f, E. Carnevali^g, P. Coufalova^h, I. Floresⁱ, O. García^j, M.A. García^k, R. González^l, A. Hernández^m, V. Inglésⁿ, G.M. Luque^b, A. Mosquera-Miguel^o, S. Pedrosa^p, M.L. Pontes^q, M.J. Porto^r, Y. Posada^s, M.I. Ramella^t, T. Ribeiro^u, E. Riego^v, A. Sala^w, V.G. Saragoni^x, A. Serrano^c, S. Vannelli^y

Participants were provided with the thresholds values used/employed: analytical threshold of 50 RFUs, stochastic threshold of 150 RFUs, and stutter threshold for each of the markers/kits according to the manufacturer's specifications.

GHEP-ISFG collaborative exercise on mixture profiles (GHEP-MIX06).

Reporting conclusions: Results and evaluation

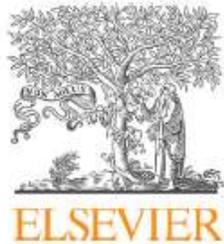
Table 1

Hypothesis and LR values obtained by each of the participating laboratories. All laboratories used the *LRmixStudio* software, except those marked as * (*EuroForMix*) and ** (*DNAMIX*). Legend: V (Victim), S (Suspect), P (Regular partner), U (Unknown).

Labs	LR value	Hypothesis	Other evaluations	
			LR value	Hypothesis
GHEPMIX_08*	1.7200E + 02	V + S + P/V + U + P		
GHEPMIX_23	2.6000E + 03	V + S + P/V + U + P		
GHEPMIX_26	6.1640E + 03	V + S + P/V + U + P		
GHEPMIX_17	6.5565E + 04	V + S + P/V + U + P		
GHEPMIX_07	6.8487E + 04	V + S + P/V + U + P		
GHEPMIX_05	1.4800E + 05	V + S + P/V + U + P		
GHEPMIX_22	2.8776E + 05	V + S + P/V + U + P		
GHEPMIX_06	3.2224E + 05	V + S + P/V + U + P		
GHEPMIX_16	4.3423E + 05	V + S + P/V + U + P		
GHEPMIX_18	1.3900E + 06	V + S + P/V + U + P		
GHEPMIX_03	1.8200E + 06	V + S + P/V + U + P		
GHEPMIX_02	2.7323E + 06	V + S + P/V + U + P		
GHEPMIX_20	5.5183E + 06	V + S + P/V + U + P		
GHEPMIX_15	1.9820E + 07	V + S + P/V + U + P		
GHEPMIX_27	1.3587E + 08	V + S + P/V + U + P	7.4048E + 19	P/U
GHEPMIX_13**	2.7300E + 10	V + S + P/V + U + P		
GHEPMIX_10	3.2032E + 14	V + S + P/V + U + P	1.1551E + 07	V + S + P/V + U1 + U2
GHEPMIX_24			1.3400E + 19	V + P/V + U

WHY DISCUSS RELIABILITY?

Forensic Science International: Genetics 37 (2018) 143–150



Contents lists available at ScienceDirect

Forensic Science International: Genetics

journal homepage: www.elsevier.com/locate/fsigen



DNA mixtures interpretation – A proof-of-concept multi-software comparison highlighting different probabilistic methods' performances on challenging samples



E. Alladio^{a,b,*}, M. Omedei^b, S. Cisana^b, G. D'Amico^b, D. Caneparo^b, M. Vincenti^{a,b}, P. Garofano^{b,c}

^a Dipartimento di Chimica, Università degli Studi di Torino, Via P. Giuria 7, 10125, Torino, Italy

^b Centro Regionale Antidoping e di Tossicologia "A. Bertinaria", Regione Gonzole 10/1, 10043, Orbassano, Torino, Italy

^c Accademia Italiana di Scienze Forensi, Viale Regina Margherita 9/D, 42124, Reggio Emilia, Italy

Lab Retriever
LRmix Studio

Page 145

DNA•VIEW®,
EuroForMix and
STRmix

Furthermore, log(LR) results provided by fully-continuous models proved similar and convergent to one another, with slightly higher within-software differences (i.e. **approximately 3–4 degrees of magnitude**).

A factor of 1000 to 10000 ?

THERE IS NO TRUE LR

Then what do the LRs offered by different labs supposed to mean?

EMPIRICAL ASSESSMENT OF LR SYSTEMS

There are two aspects to judging the reliability of a LR system for assessing value of forensic DNA evidence

1. **Accuracy** of Claim or **Calibration**

2. **Discrimination** power

H_p : DNA from POI is in the sample

H_d : DNA from POI is not in the sample

ACCURACY/CALIBRATION

LR value of x is x times more likely to occur under H_p than under H_d .

- LR value of 1 occurs as often under H_p as under H_d
- LR value of 10 occurs 10 times more often under H_p as it does under H_d .
- LR value of 100 occurs 100 times more often under H_p as it does under H_d .
- LR value of 0.1 occurs 10 times more often under H_d as it does under H_p .
- And, in general, whether a LR value of x occurs (roughly) x times more often under H_p than under H_d .

ACCURACY/CALIBRATION

LR value of x is x times more likely to occur under H_p than under H_d .

(**LR of LR is LR**)

..... the likelihood ratio of the likelihood ratio is the likelihood ratio. That is

$$l[l(e_k)] = \frac{P_1[l(e_k) | h_1]}{P_2[l(e_k) | h_2]} = l(e_k) \quad (1.32)$$

for all events e_k .

Green and Swets, 1966, page 26, section 1.8, equation (1.32)

In principle, this property can be empirically tested

ACCURACY/CALIBRATION – EMPIRICAL ASSESSMENT

- Suppose we have a large collection of ground truth known DNA samples representing different scenarios (degradation, number of contributors, template amounts) we expect to encounter in case work
- For each sample, select a known contributor profile or a known noncontributor profile (say by coin toss) and **send them through the LR pipeline, from analysis to interpretation.** (blinded)
- Record the value of LR obtained along with whether it is for H_p true case or for a H_d true case.
- At the end of this exercise we will have a pool of H_p true LR values and a pool of H_d true LR values.

Don't Try This At Home !

"I TRIED IT AT HOME..."



Disclaimer:

This is only a thought experiment.

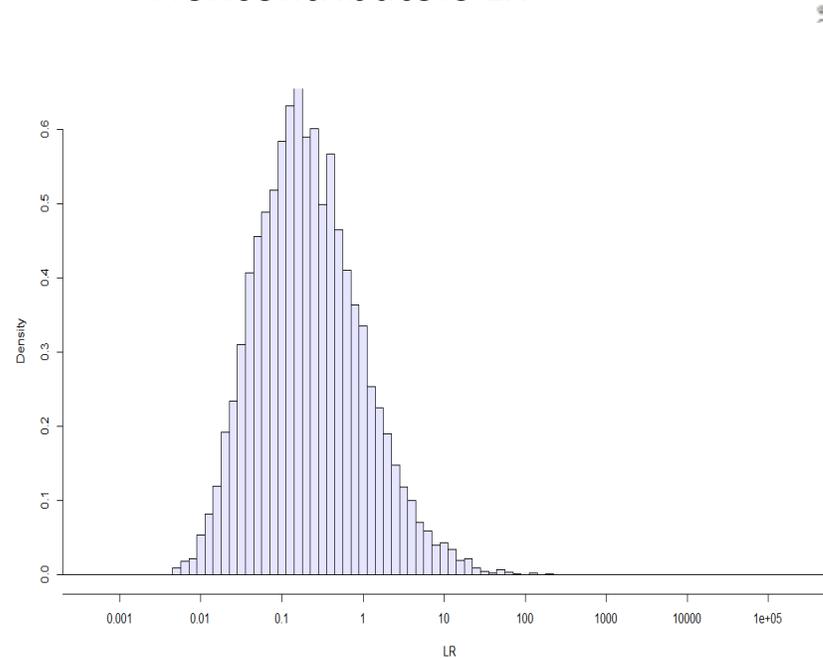
Actual assessment will require a well thought out experimental design and lots of

\$\$

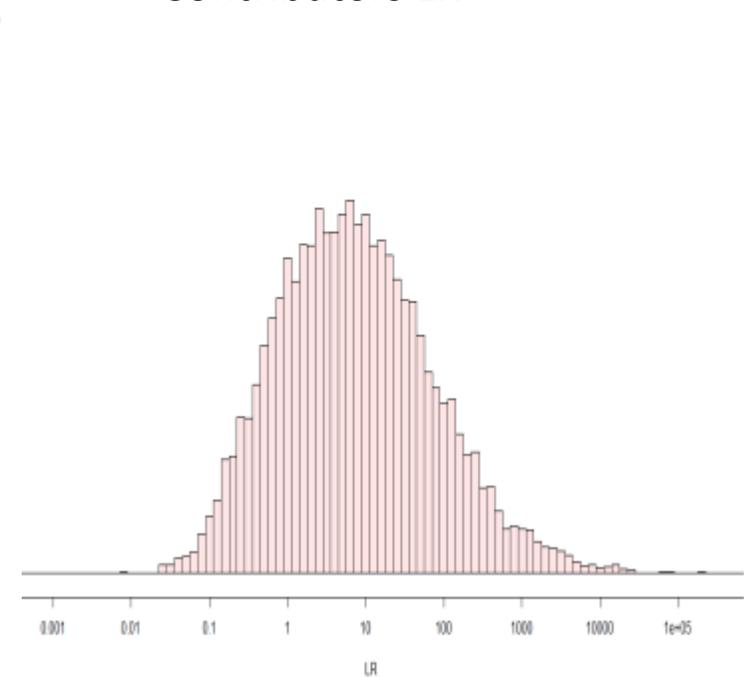
ACCURACY/CALIBRATION – EMPIRICAL ASSESSMENT

Known Noncontributors LR	Known Contributors LR
0.00E+00	3.68E+08
6.69E-03	2.10E+07
1.48E-03	7.34E+10
1.60E-03	1.26E+09
1.04E+00	1.45E+08
0.00E+00	3.87E+10
1.32E-01	3.12E+07
3.98E-03	1.71E+06
1.12E-02	6.56E+10
1.85E-06	1.95E+08
1.56E-01	1.61E+06
5.48E-09	4.13E+10
3.97E-04	1.87E+08
0.00E+00	1.11E+06
6.07E-13	5.18E+09
5.03E-04	2.99E+07
7.10E-03	1.87E+05
0.00E+00	1.86E+09
0.00E+00	8.08E+08
5.81E-01	7.17E+17
8.81E-08	5.81E+13
1.32E-01	2.76E+09
2.26E-14	3.18E+17
2.12E-01	4.66E+13
2.78E-01	4.78E+07
ETC	
1.21E+00	1.01E+17
1.09E-03	1.16E+12
2.09E-13	1.41E+06
0.00E+00	9.87E+16
0.00E+00	2.61E+10
2.60E-01	2.34E+03
1.37E-04	1.05E+16

Noncontributors LR



Contributors LR



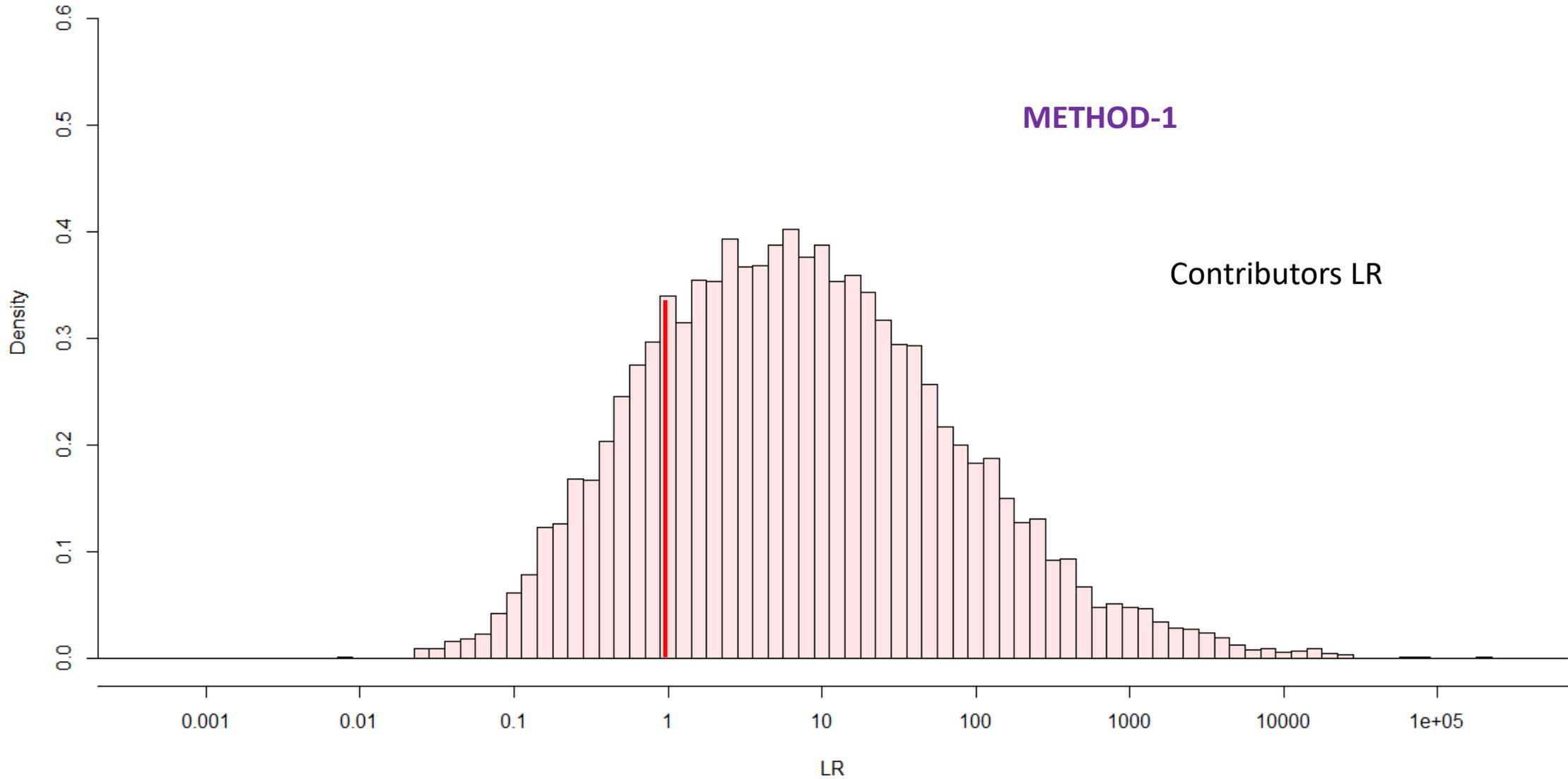
Disclaimer: This is only a thought experiment.

Actual assessment will require a well thought out experimental design.

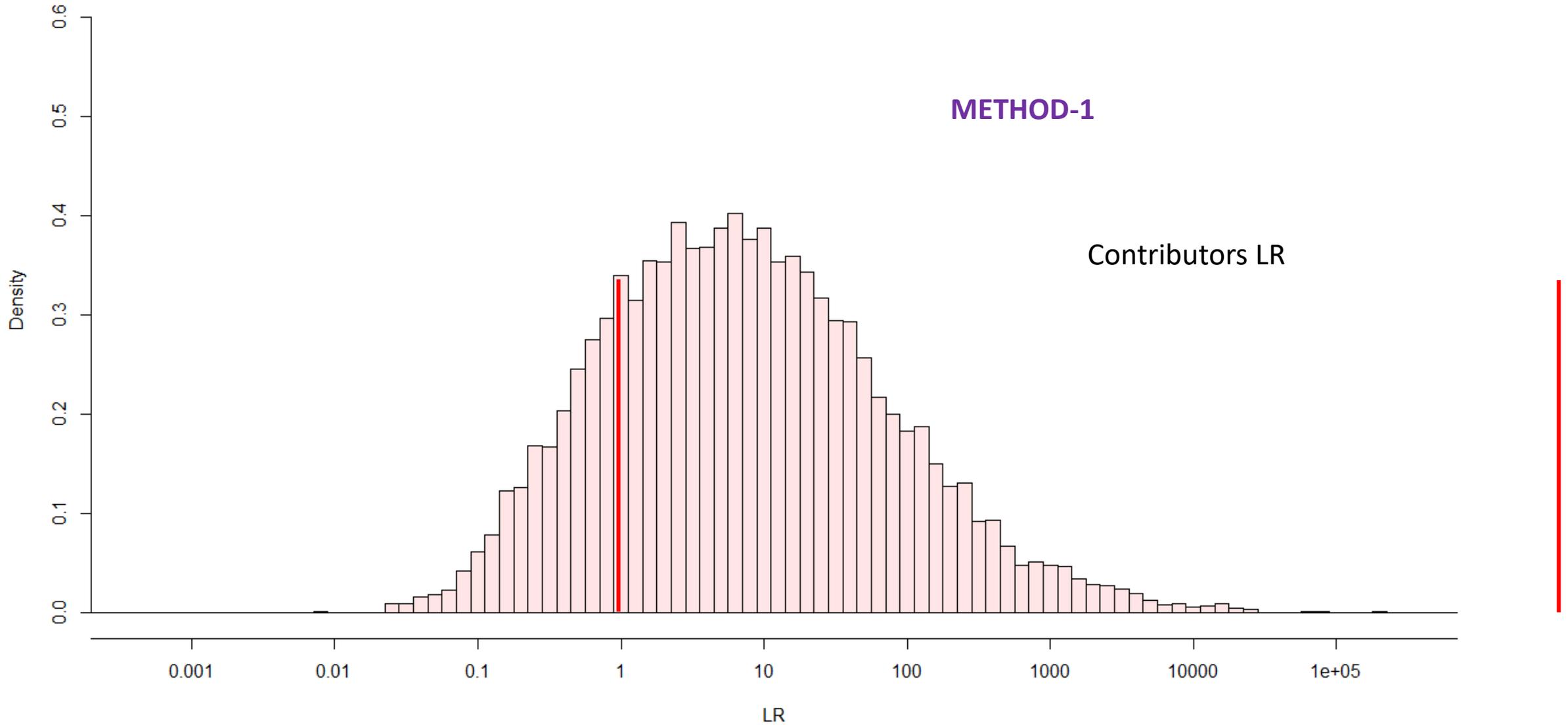
ACCURACY/CALIBRATION

- check whether a LR value of 1 occurs (roughly) equally often under H_p as well as under H_d
- check whether a LR value of 10 occurs (roughly) 10 times more often under H_p as it does under H_d .
- Check whether a LR value of 100 occurs (roughly) 100 times more often under H_p as it does under H_d .
- Check whether a LR value of 0.1 occurs (roughly) 10 times more often under H_d as it does under H_p .
- And, **in general, whether a LR value of x occurs (roughly) x times more often under H_p than under H_d .**

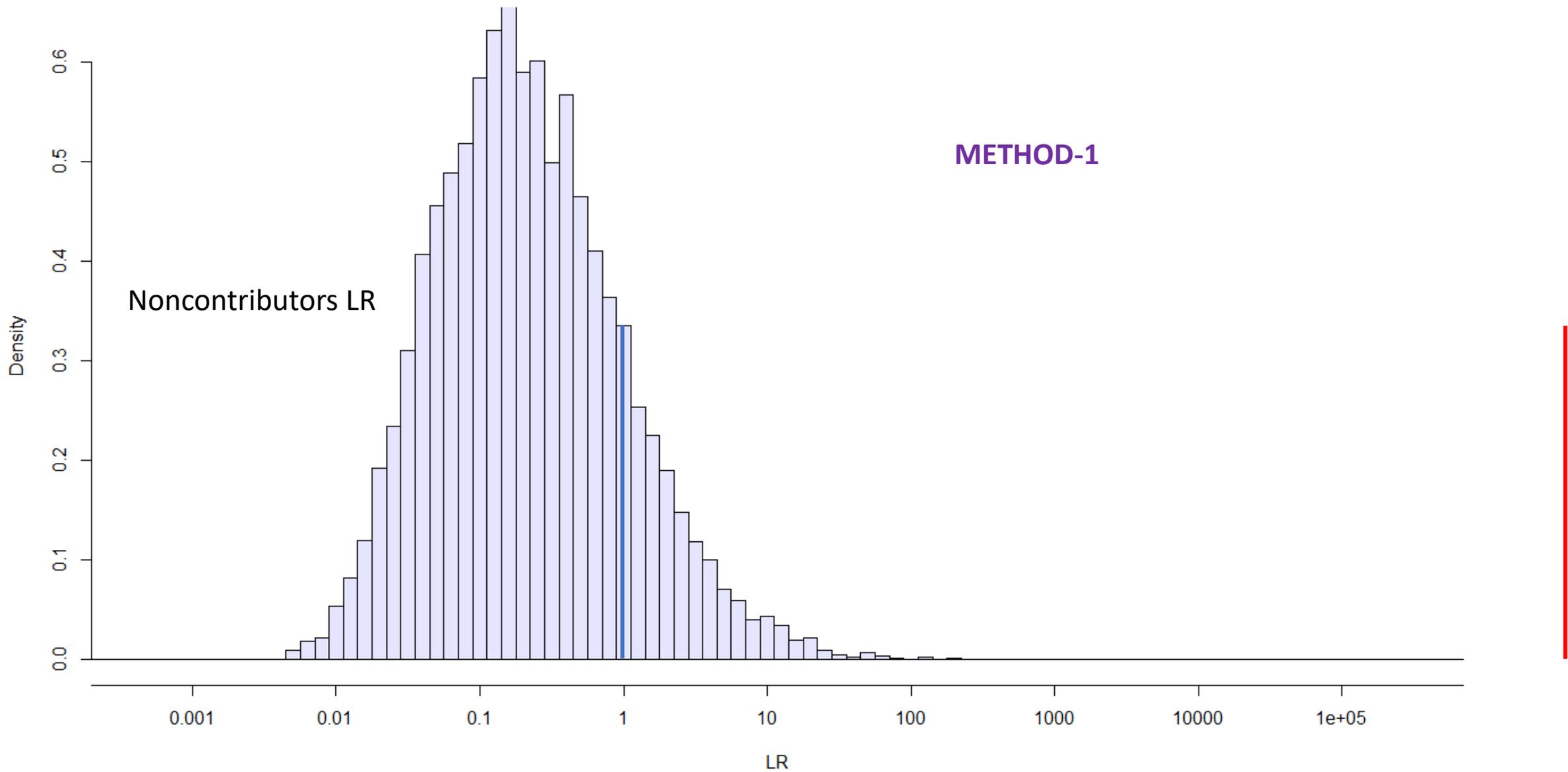
ACCURACY/CALIBRATION – EMPIRICAL ASSESSMENT



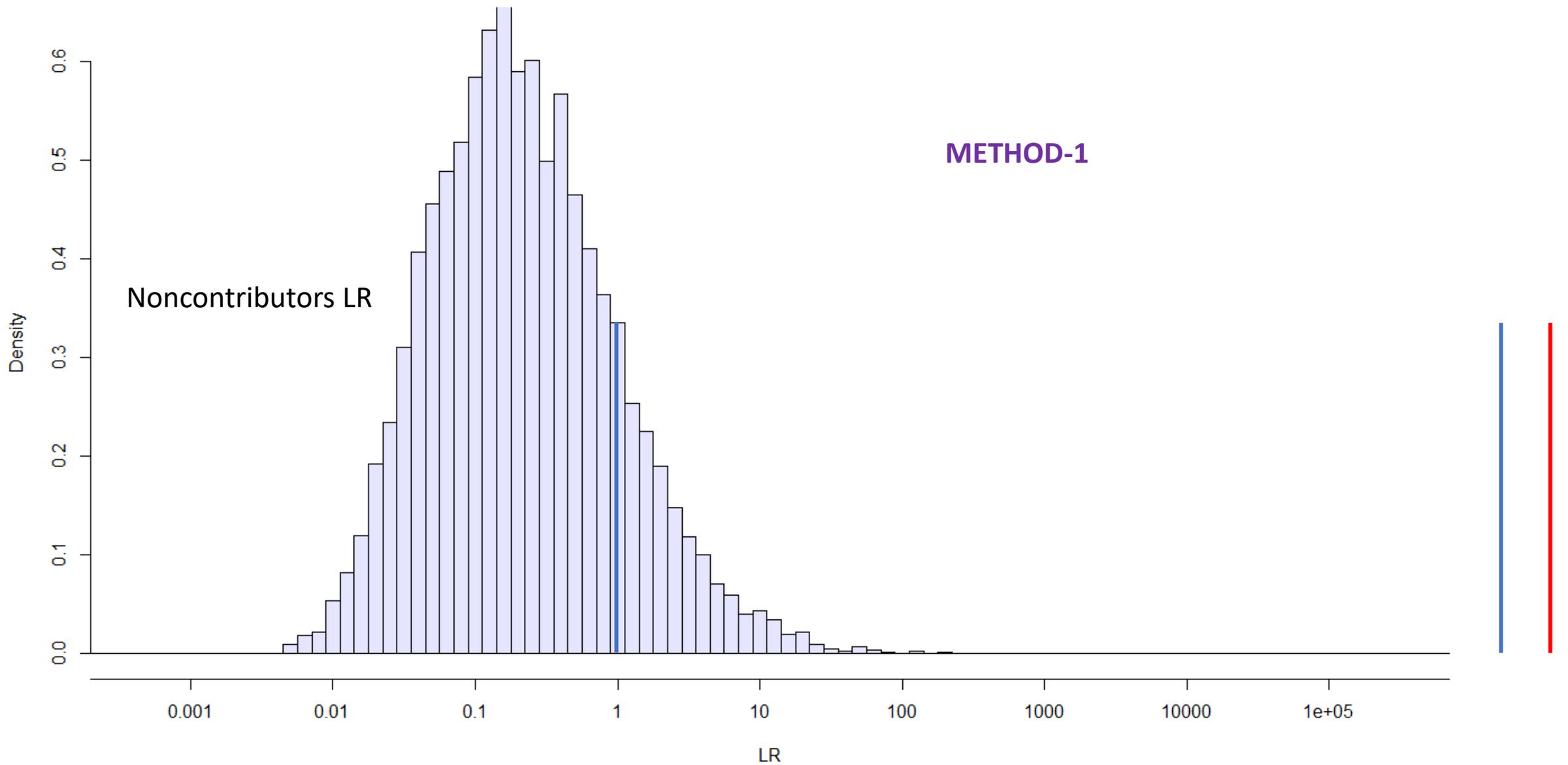
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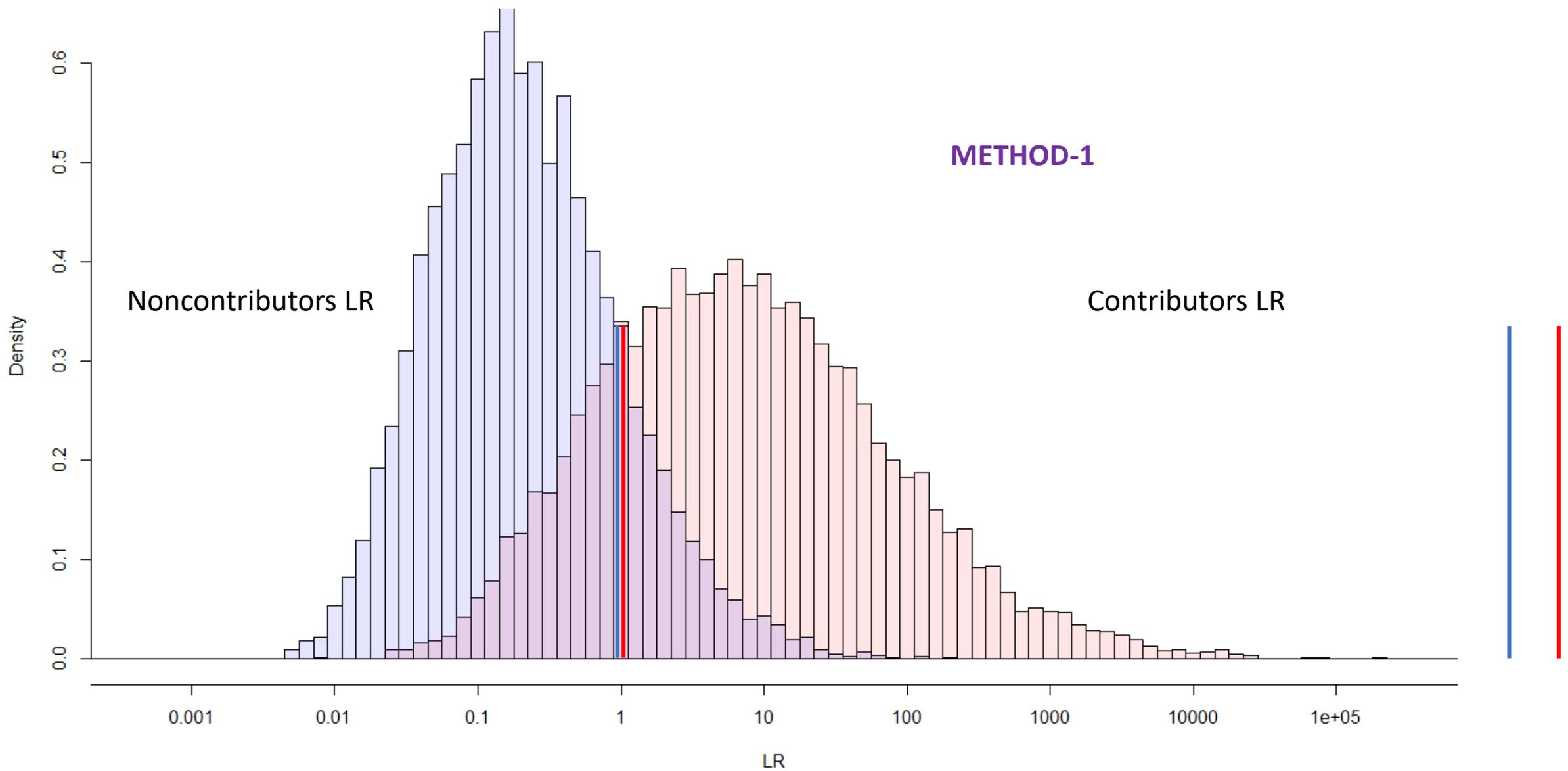
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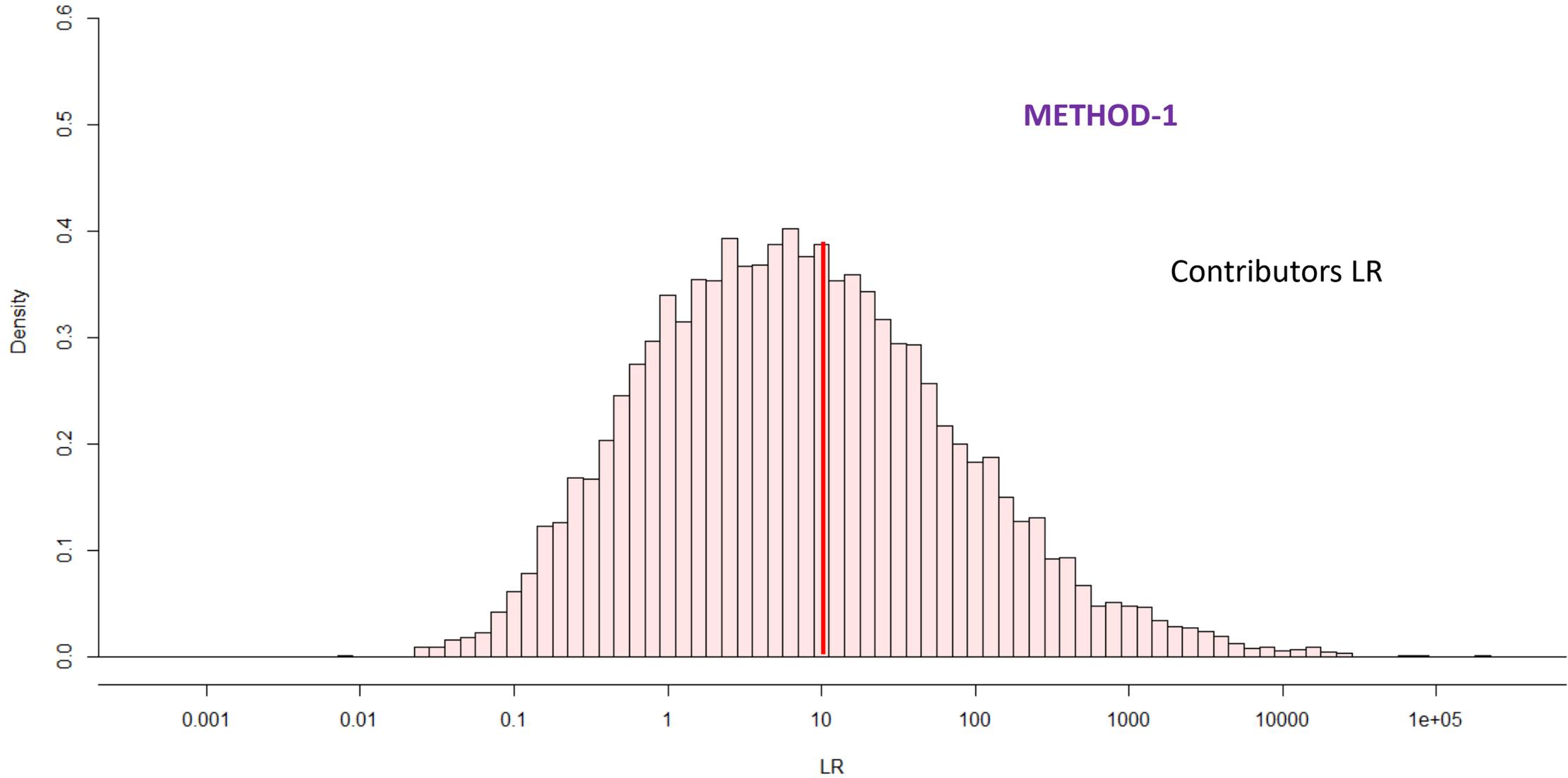
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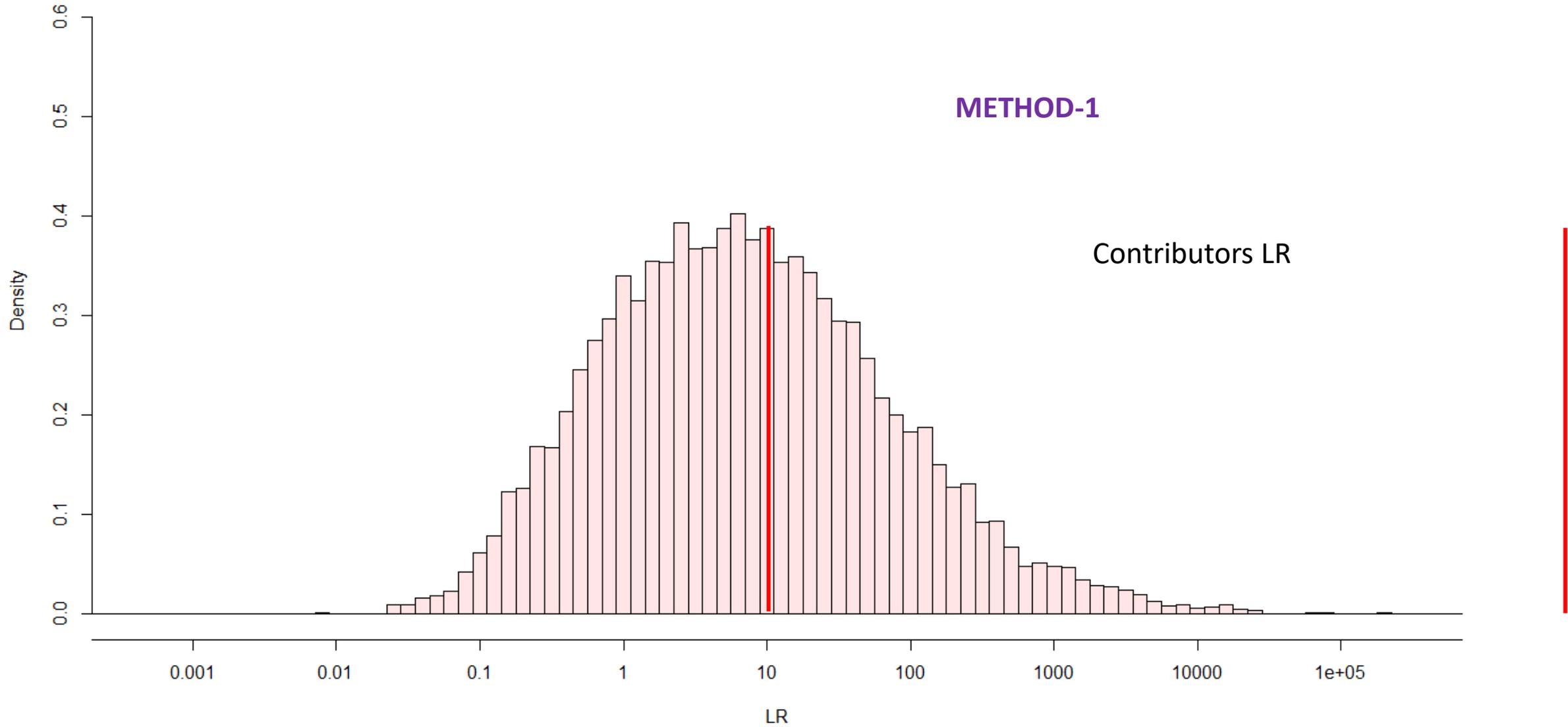
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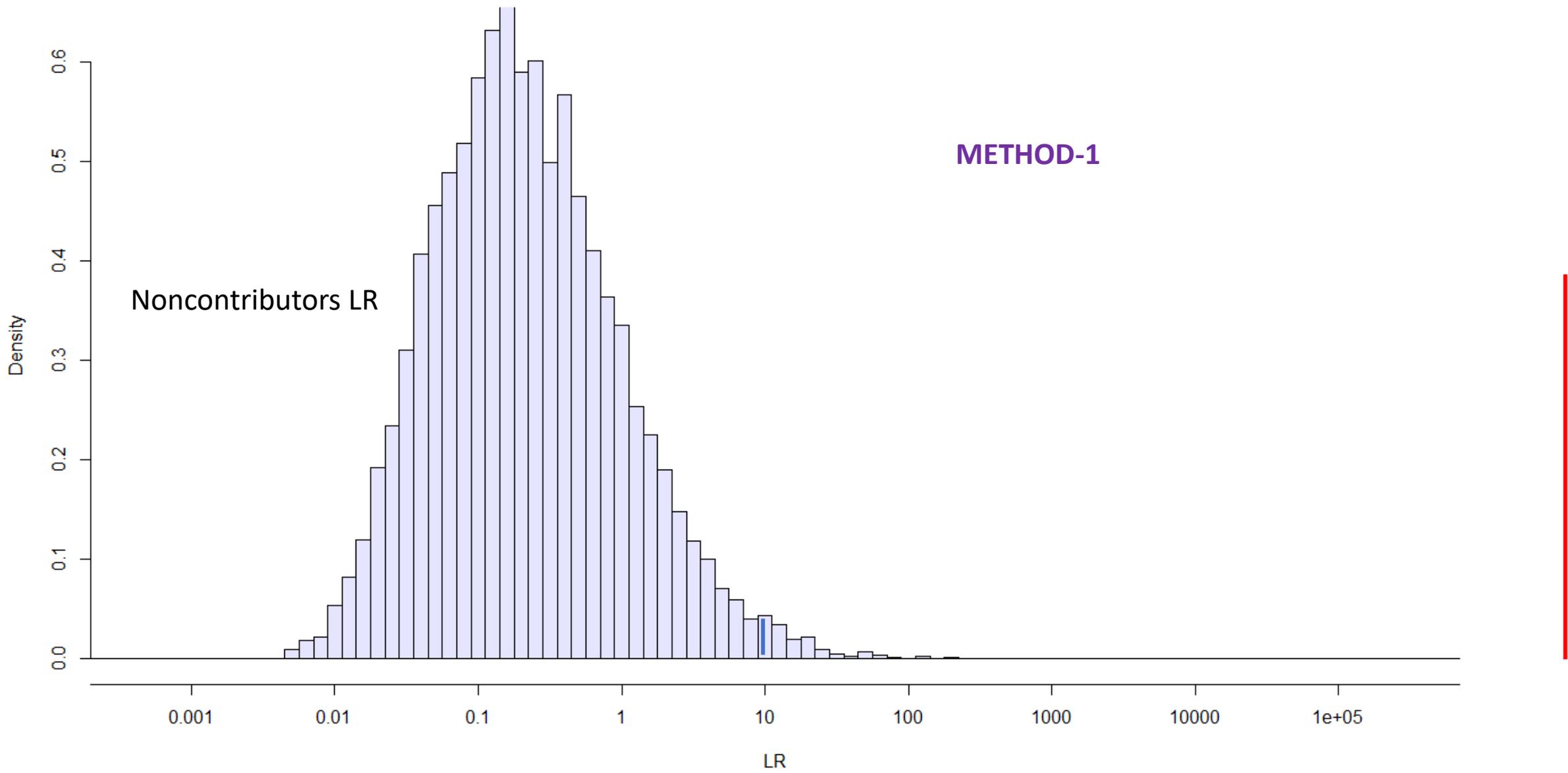
ACCURACY/CALIBRATION – EMPIRICAL ASSESSMENT



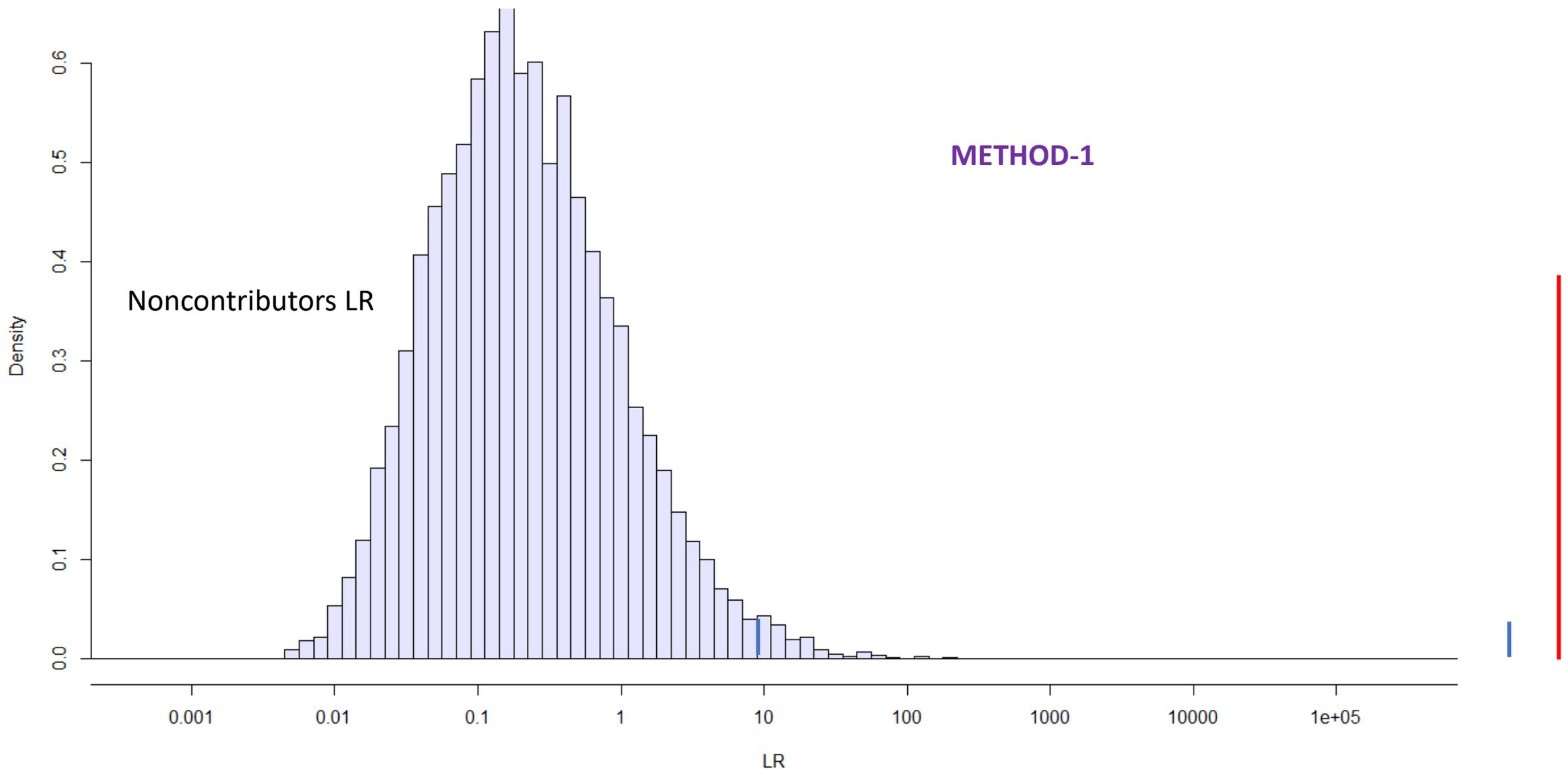
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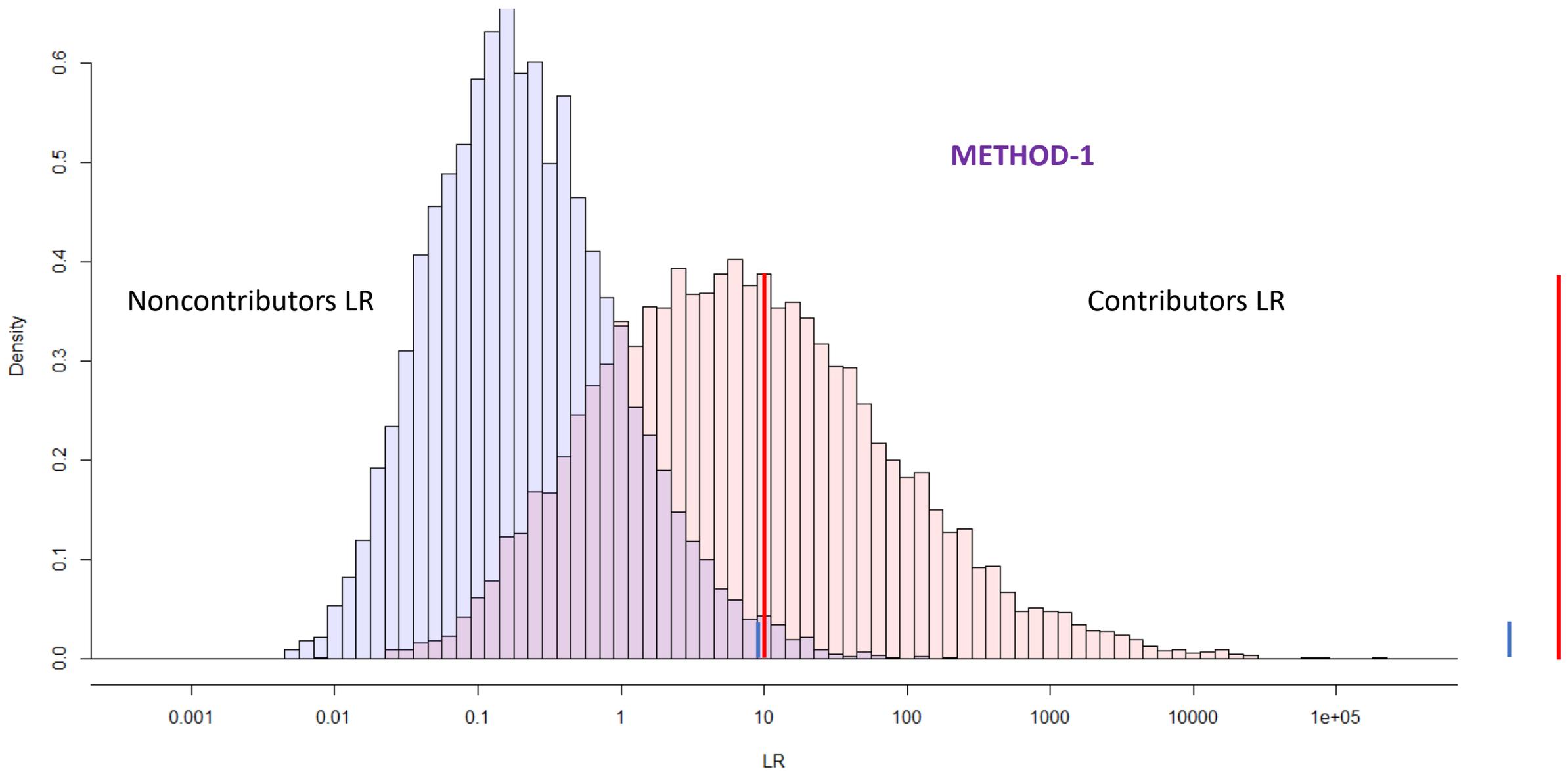
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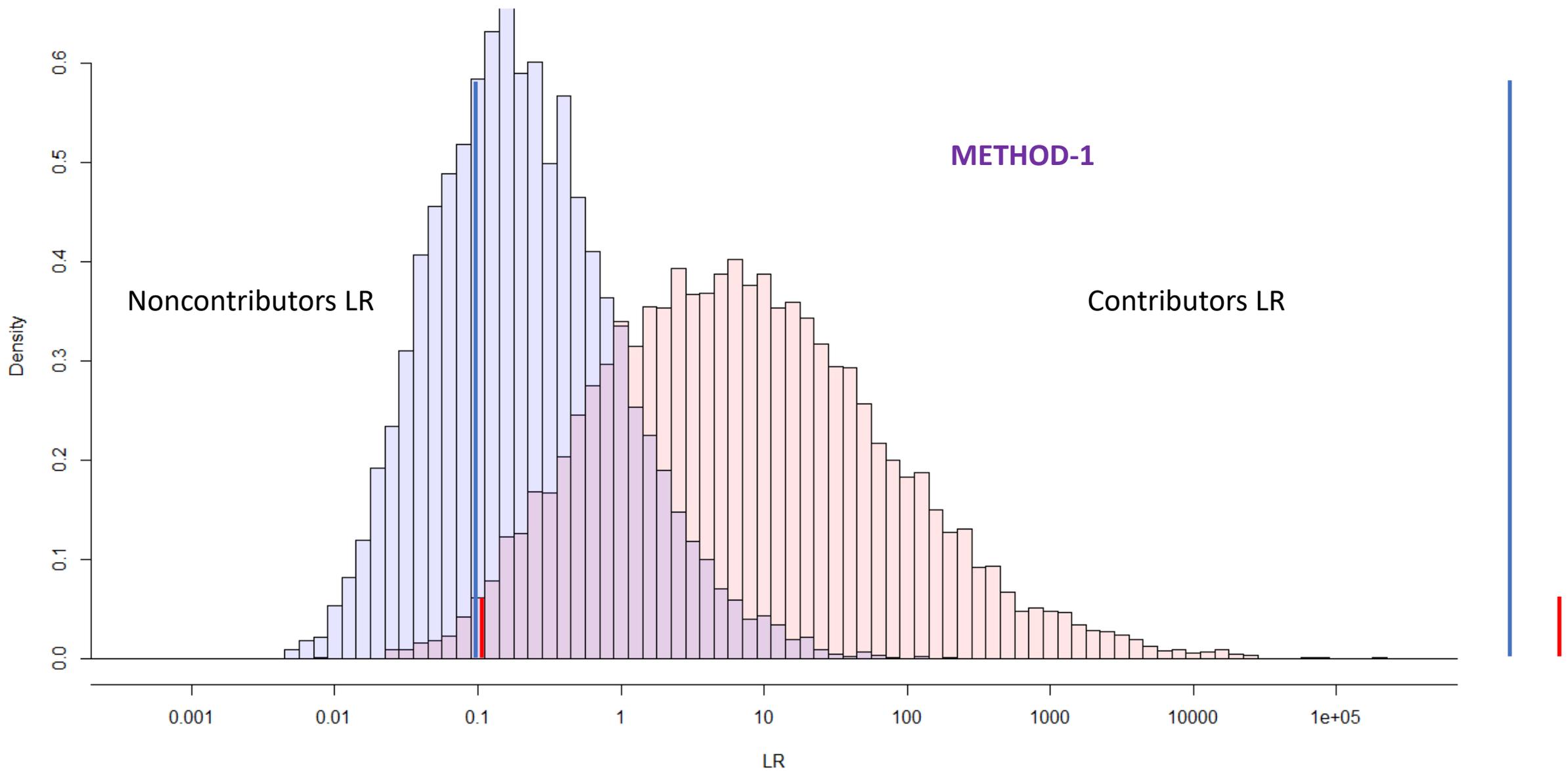
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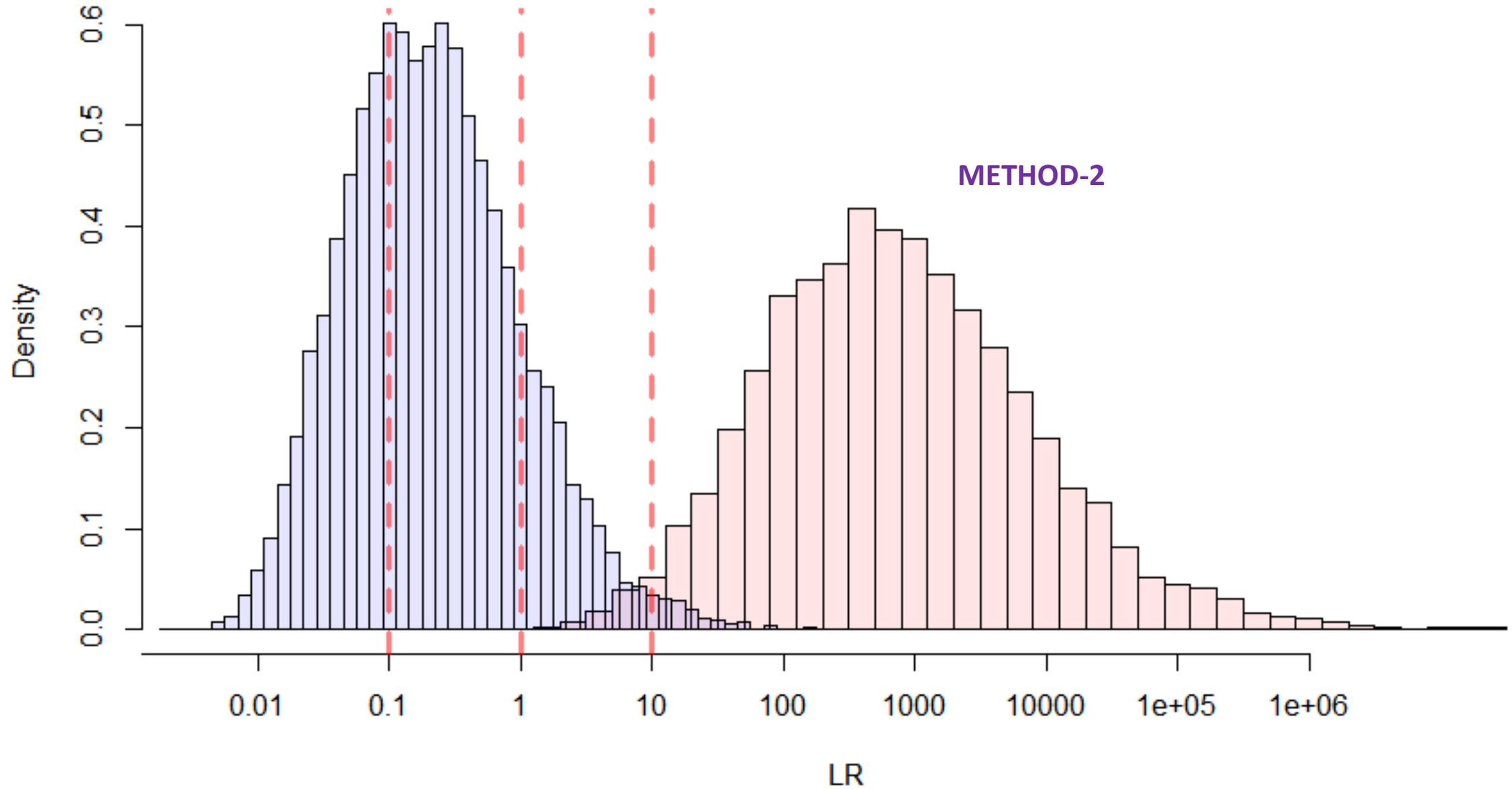
ACCURACY/CALIBRATION – EMPIRICAL ASSESSMENT



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ACCURACY/CALIBRATION – EMPIRICAL ASSESSMENT

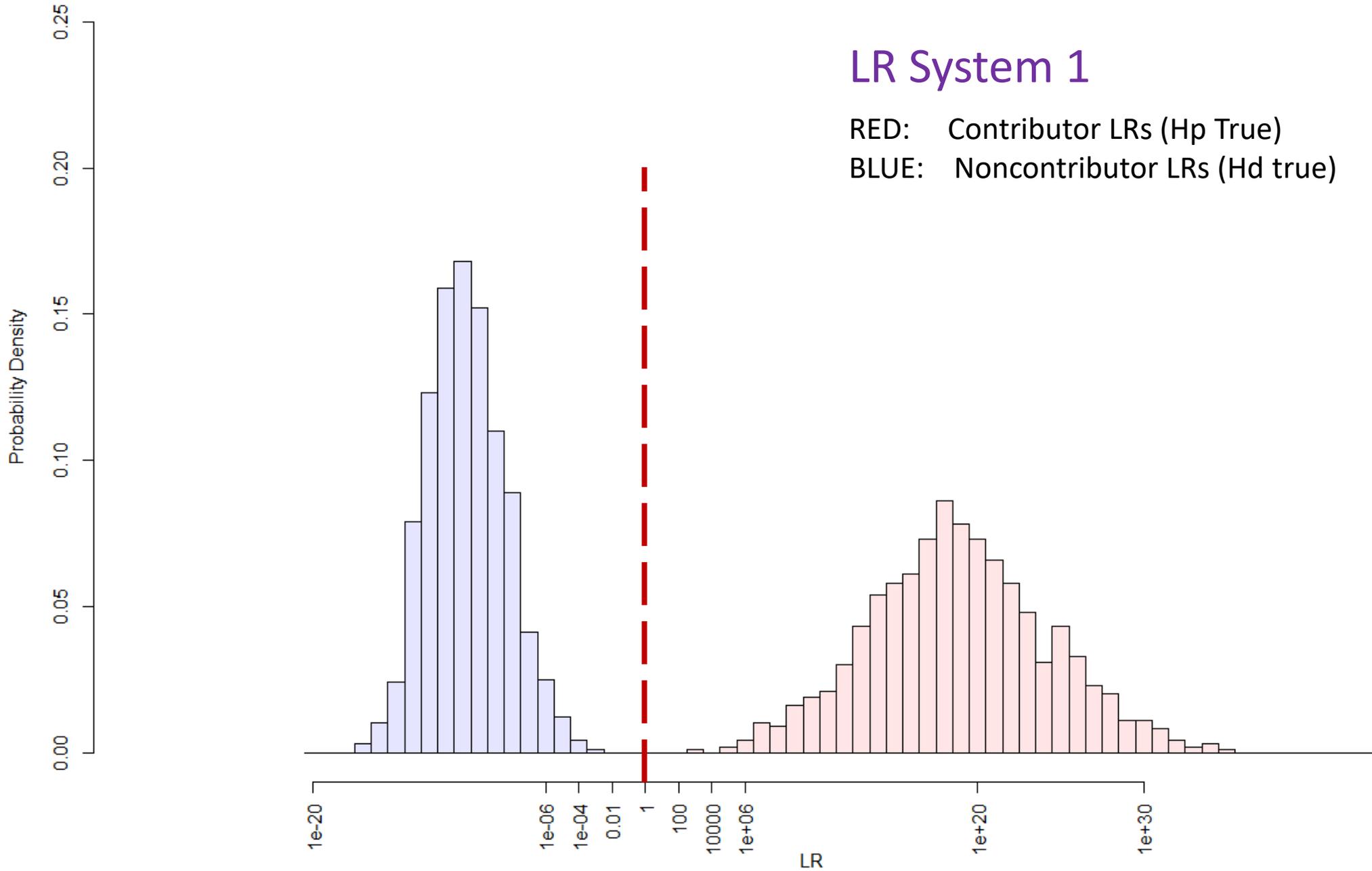


DISCRIMINATING POWER

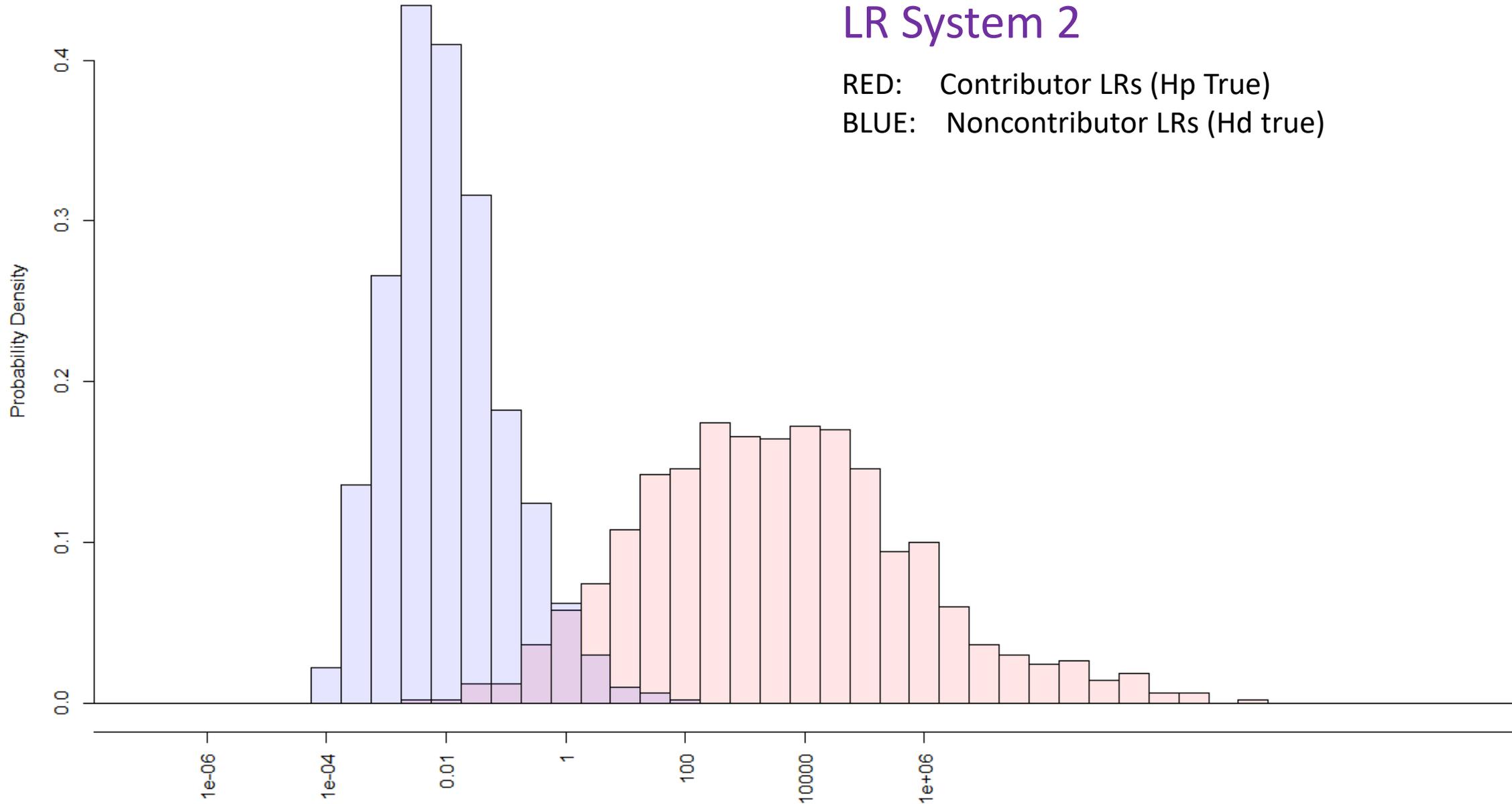
The ability of an LR system to discriminate between H_p and H_d depends on

1. How much of the discriminating information in the sample is measured and used in the interpretation?
2. Do the models used to incorporate such information represent reality adequately?

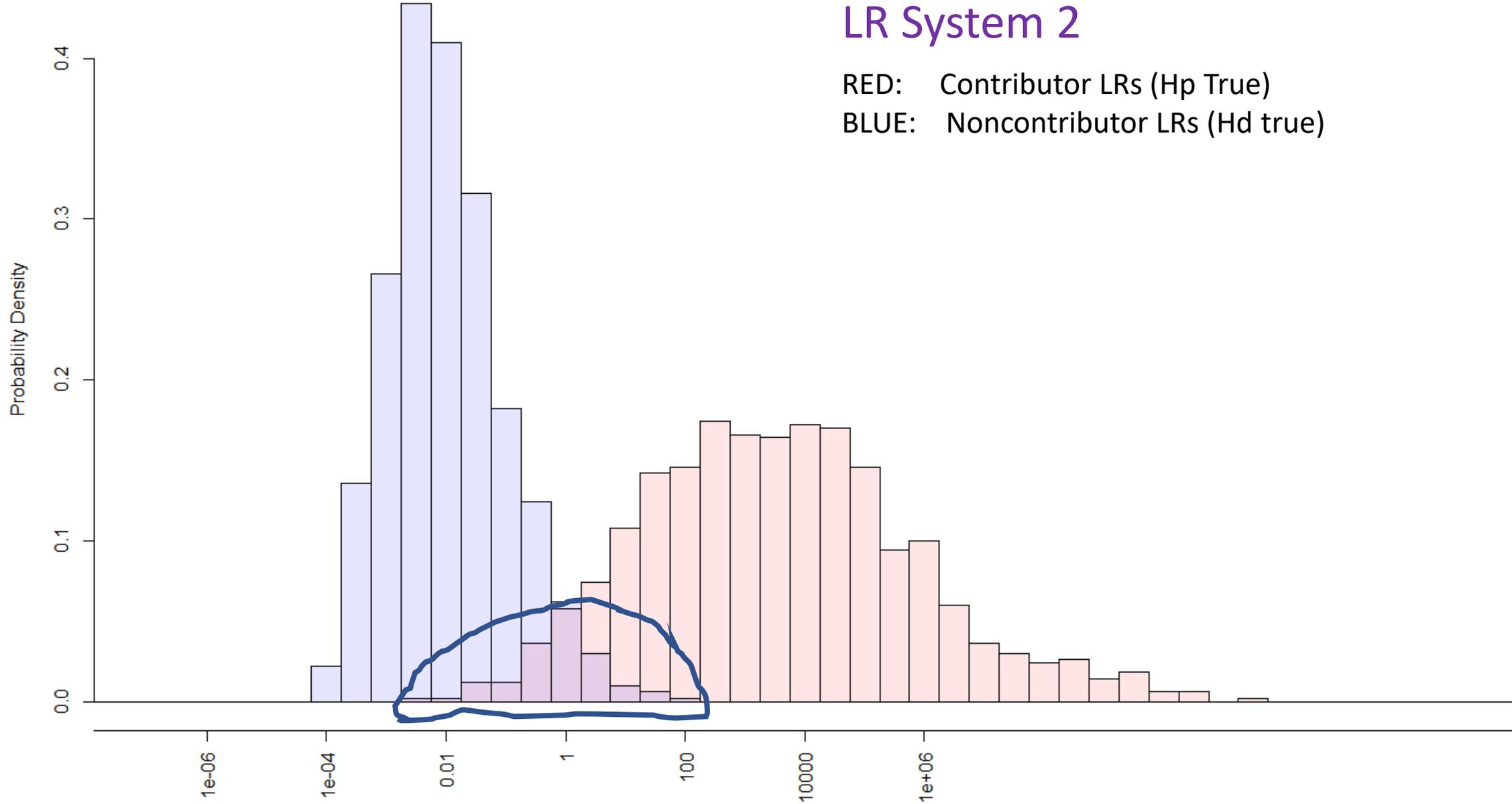
DISCRIMINATION POWER



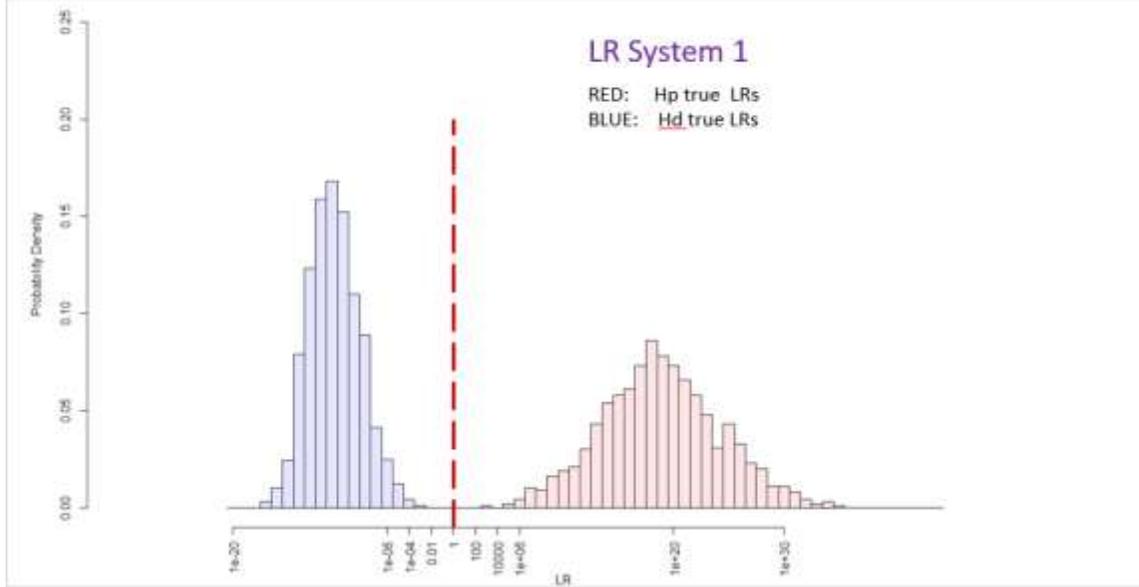
DISCRIMINATION POWER



DISCRIMINATION POWER

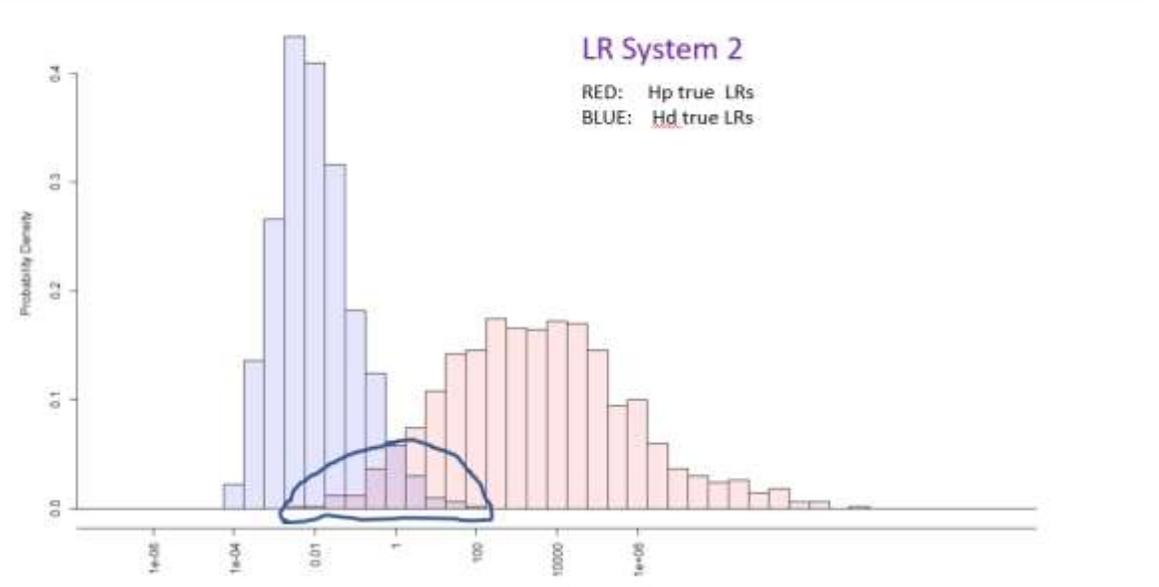


DISCRIMINATION POWER



LR System 1

DISCRIMINATION POWER



LR System 2

LR System 1 is more discriminating between H_p and H_d than LR system 2

TIPPETT PLOTS

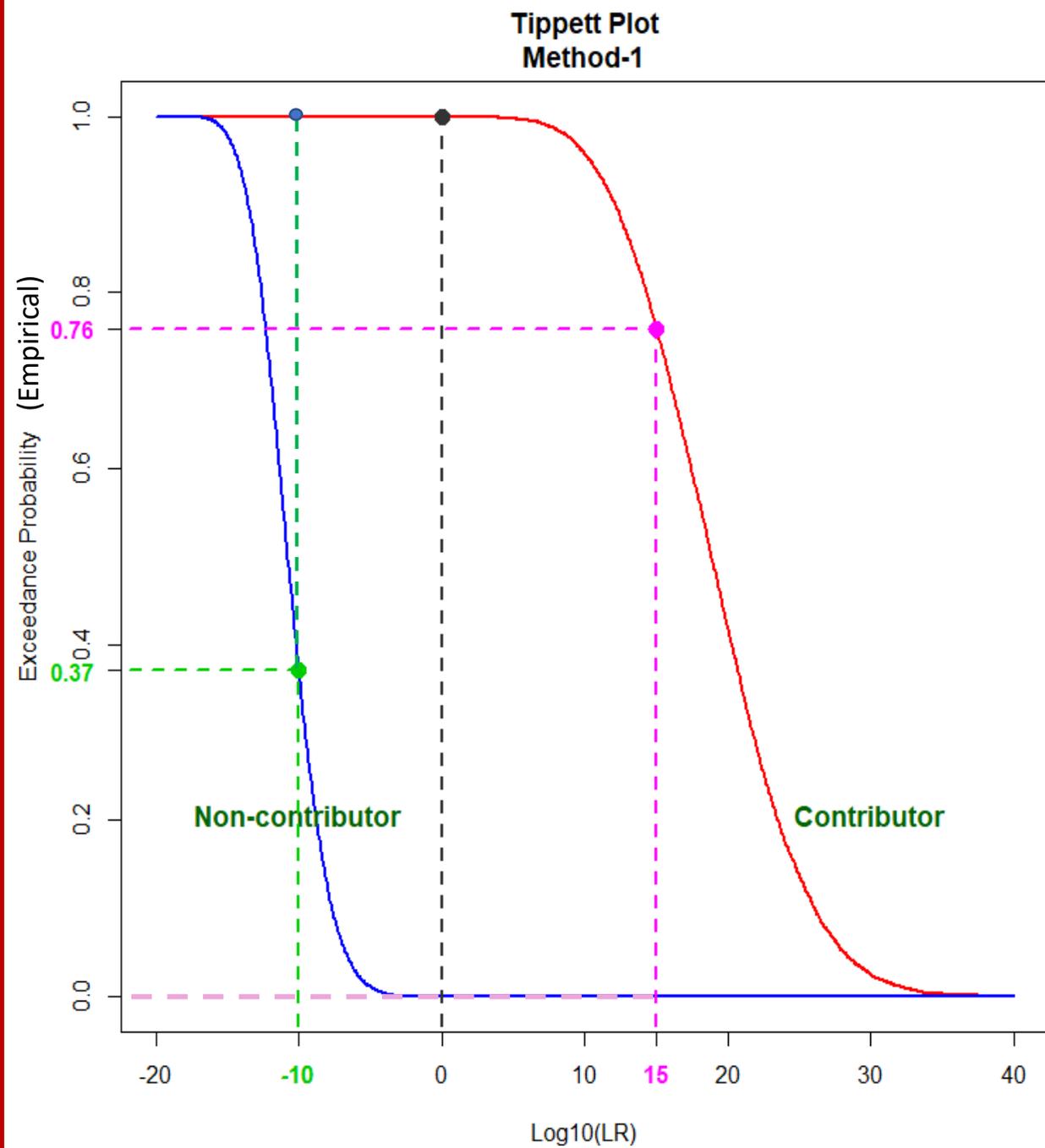
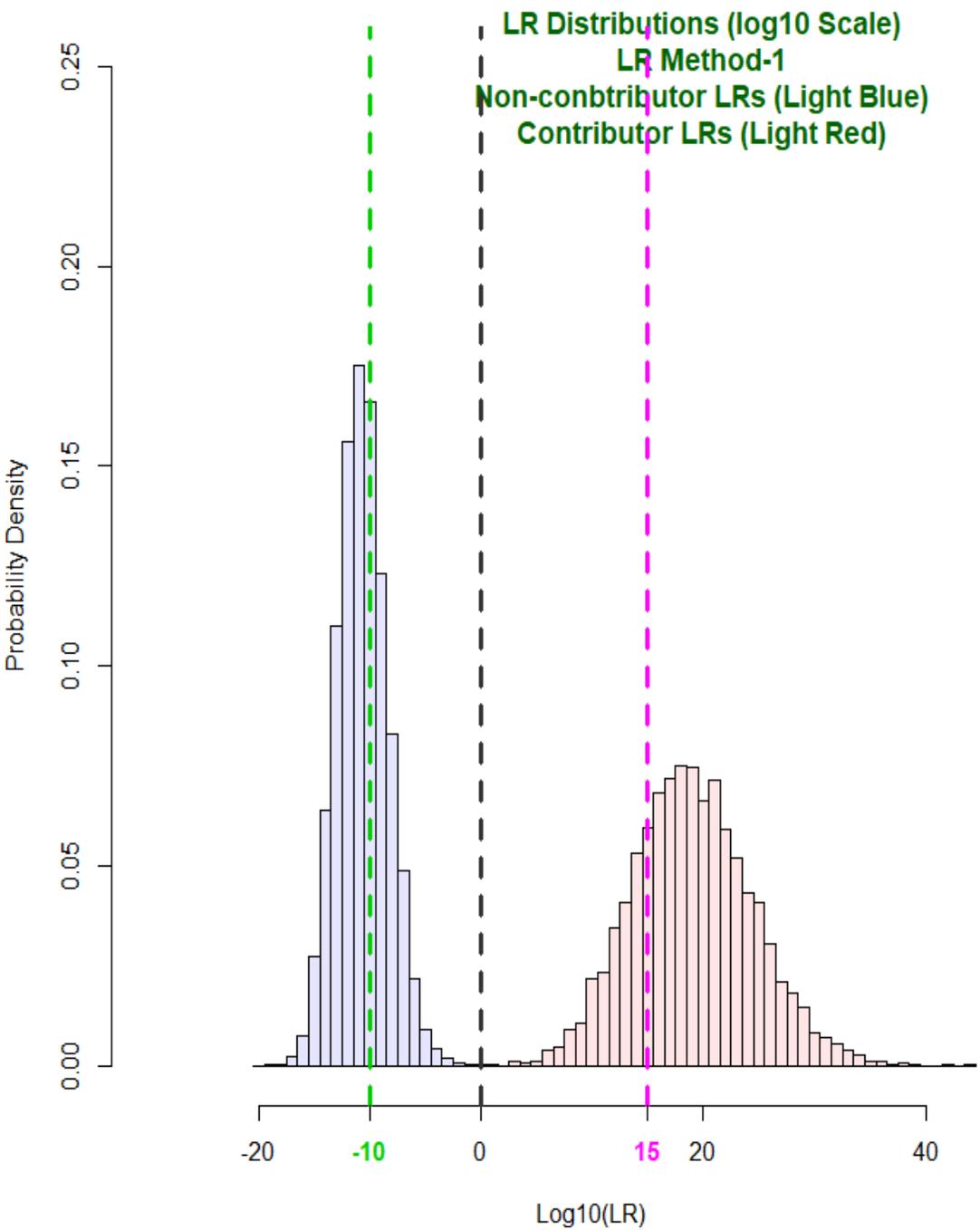
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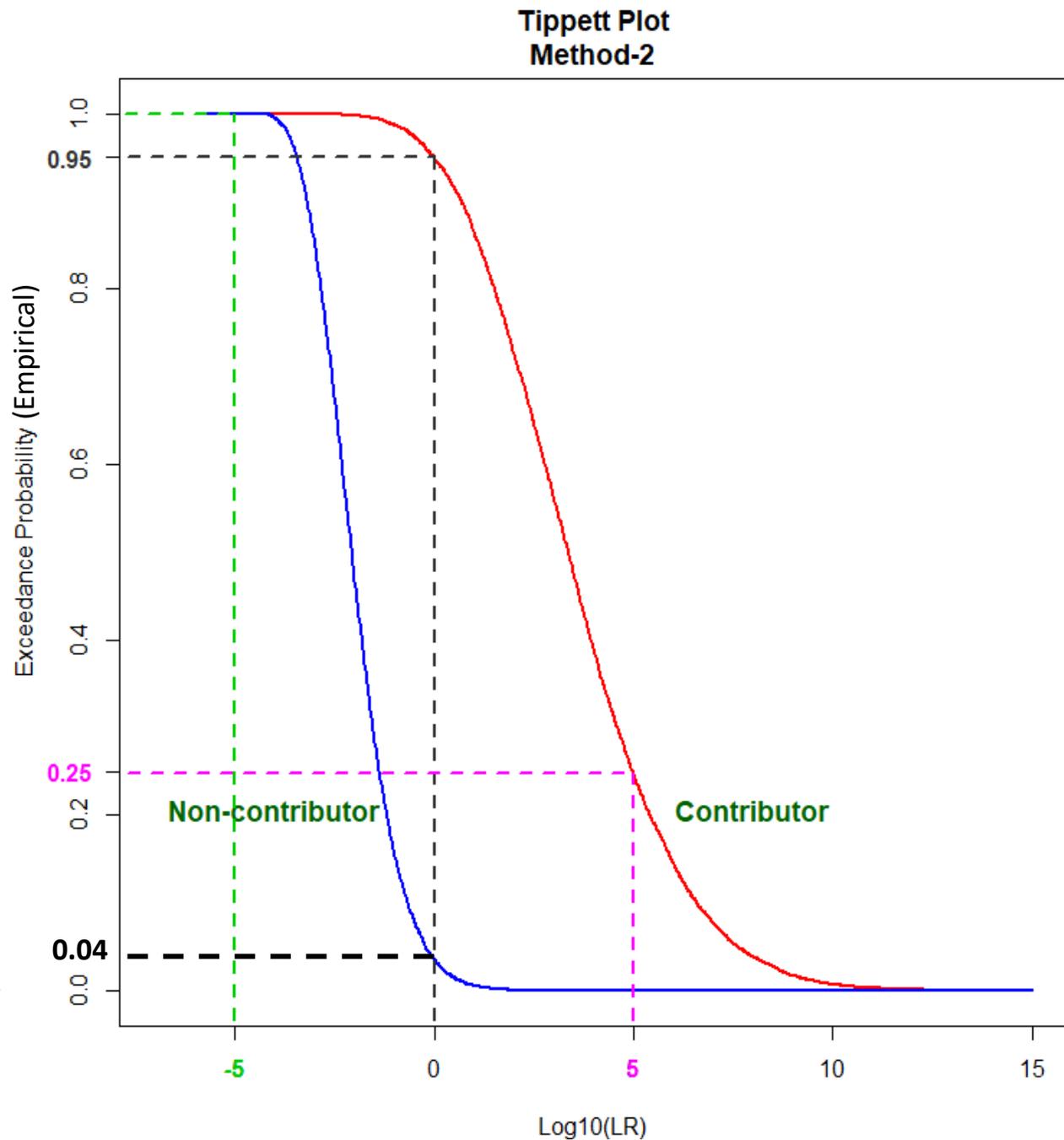
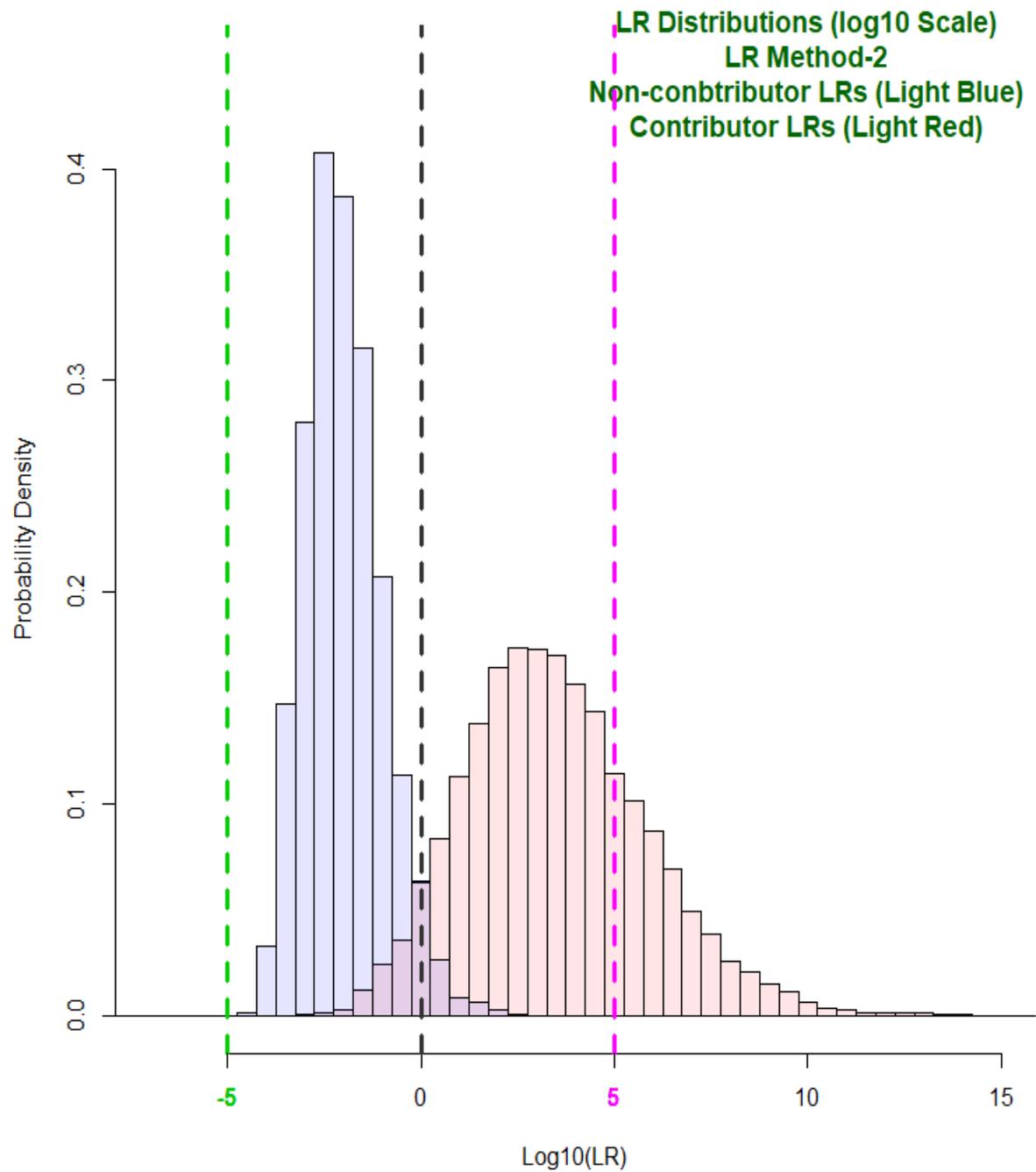
I.W.Evett¹ and J.S.Buckleton²

Advances in Forensic Haemogenetics 6

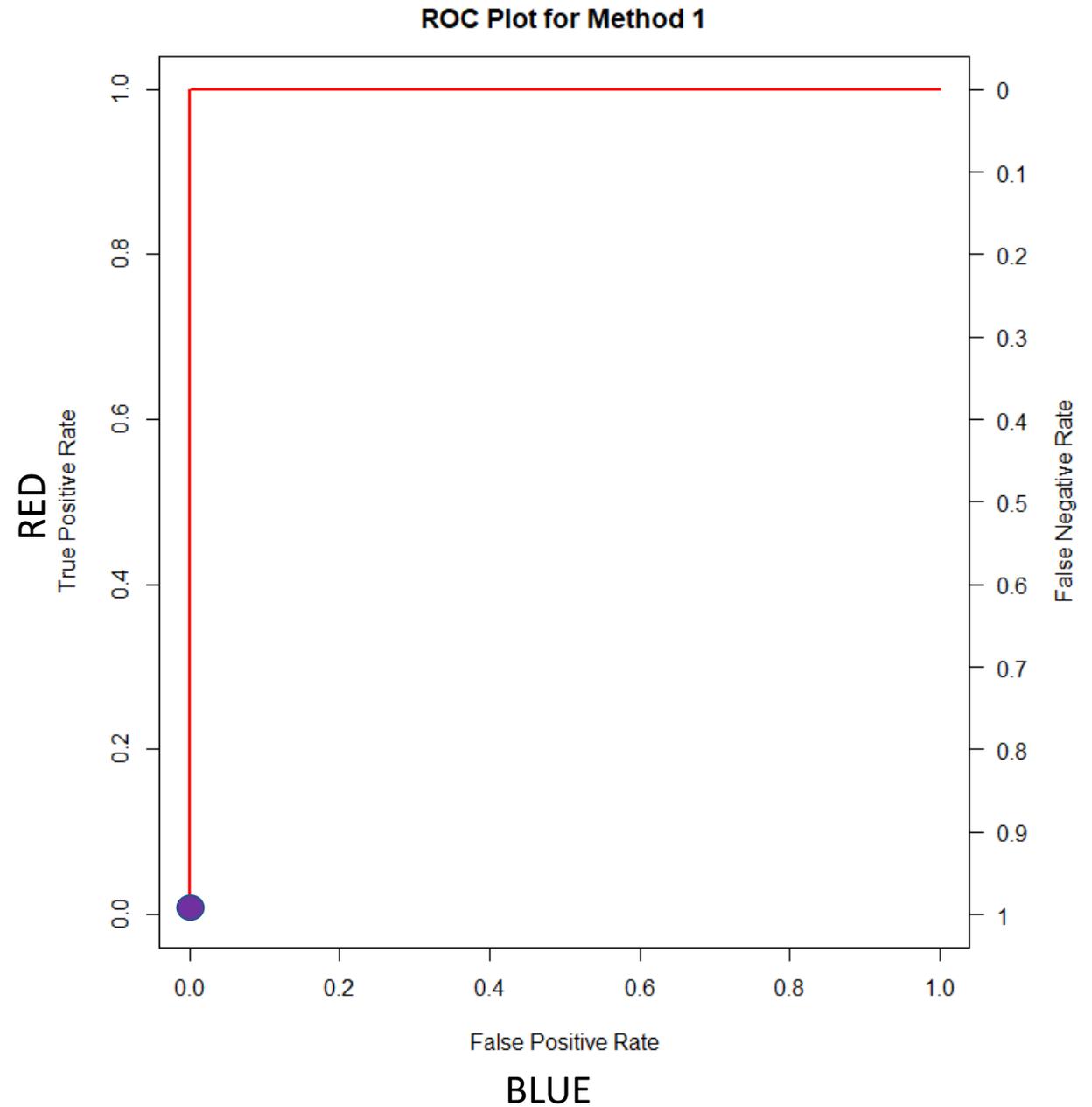
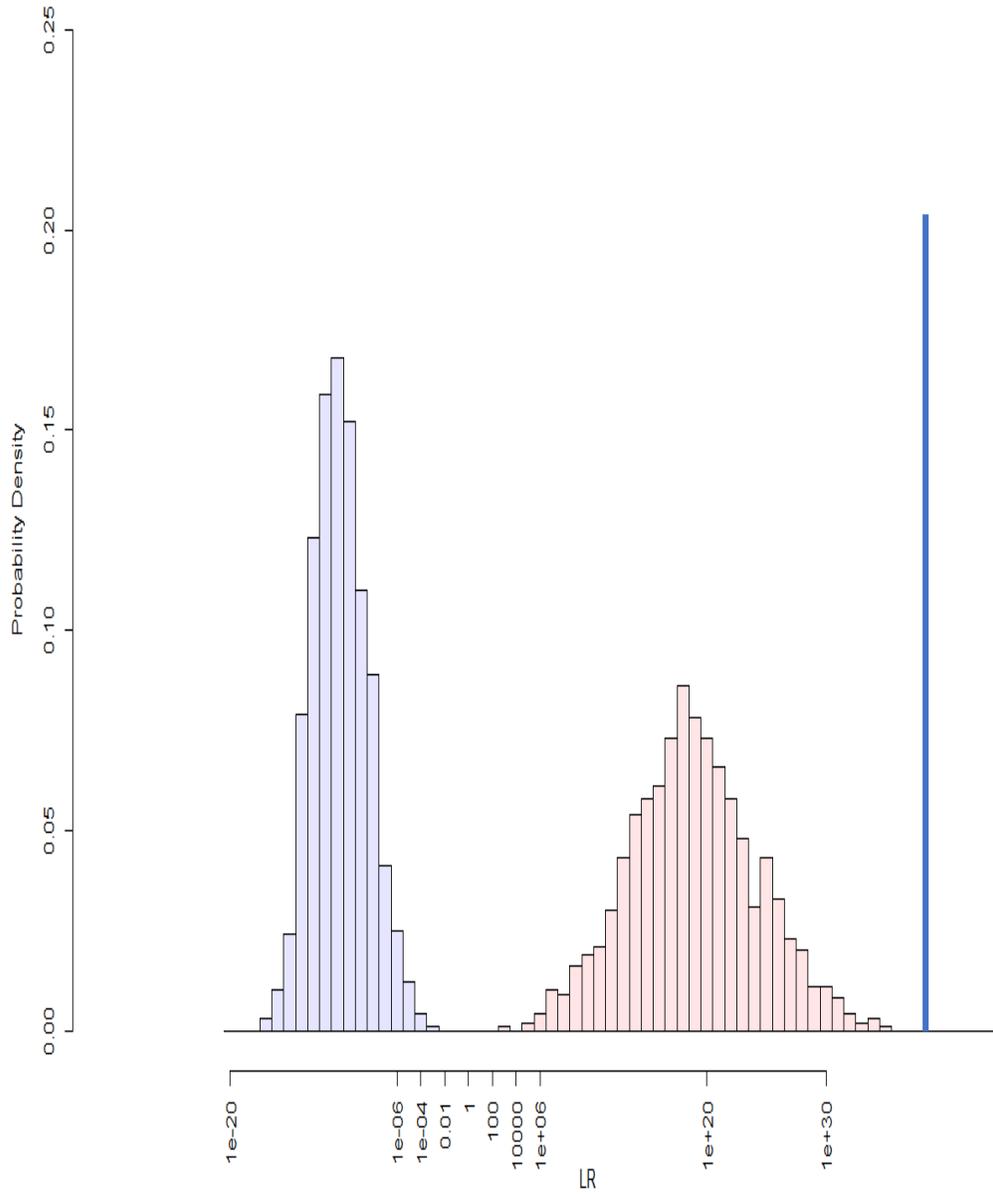
16th Congress of the
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(Internationale Gesellschaft für forensische Hämogenetik e.V.)
Santiago de Compostela, 12-16 September 1995

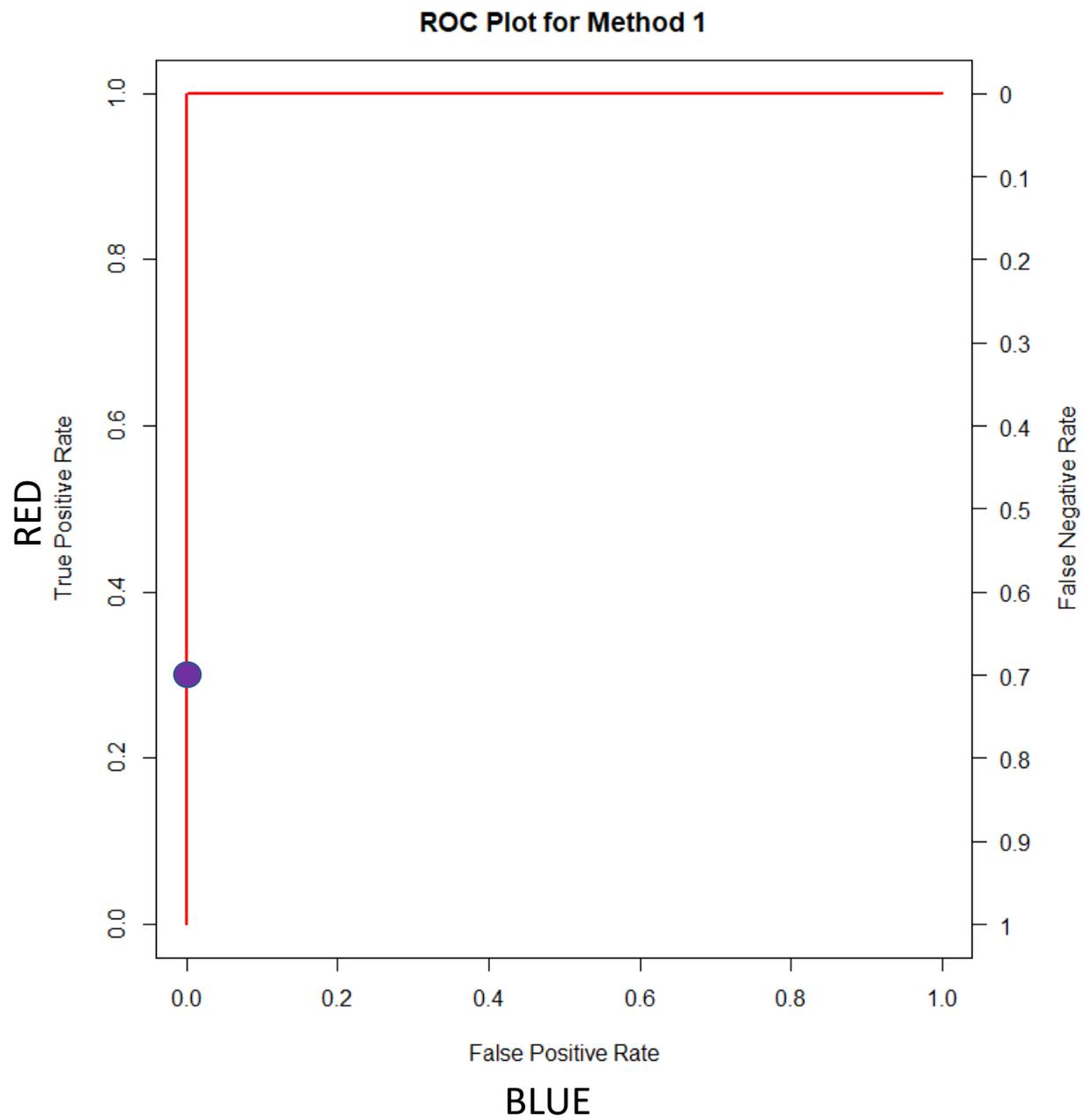
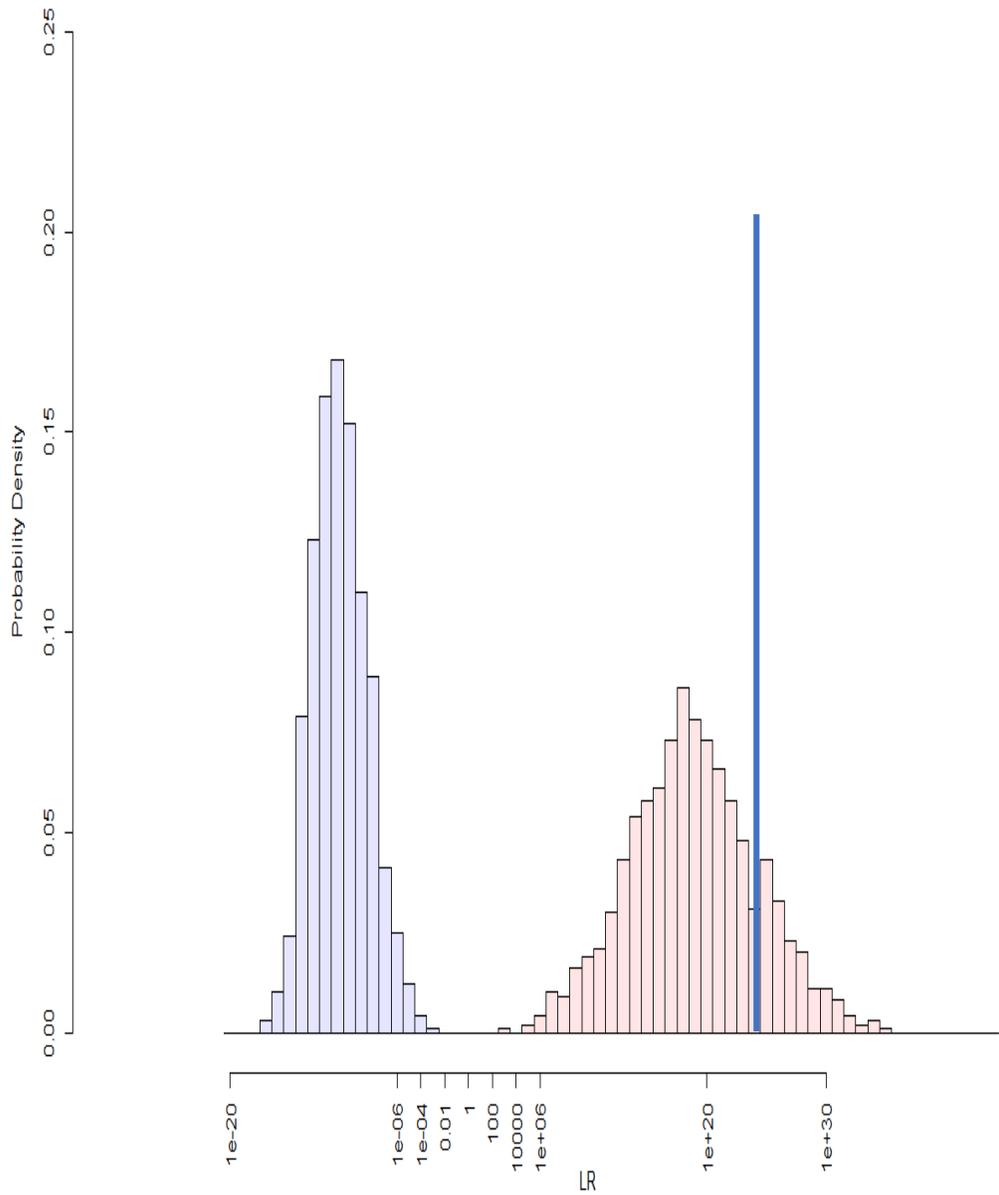
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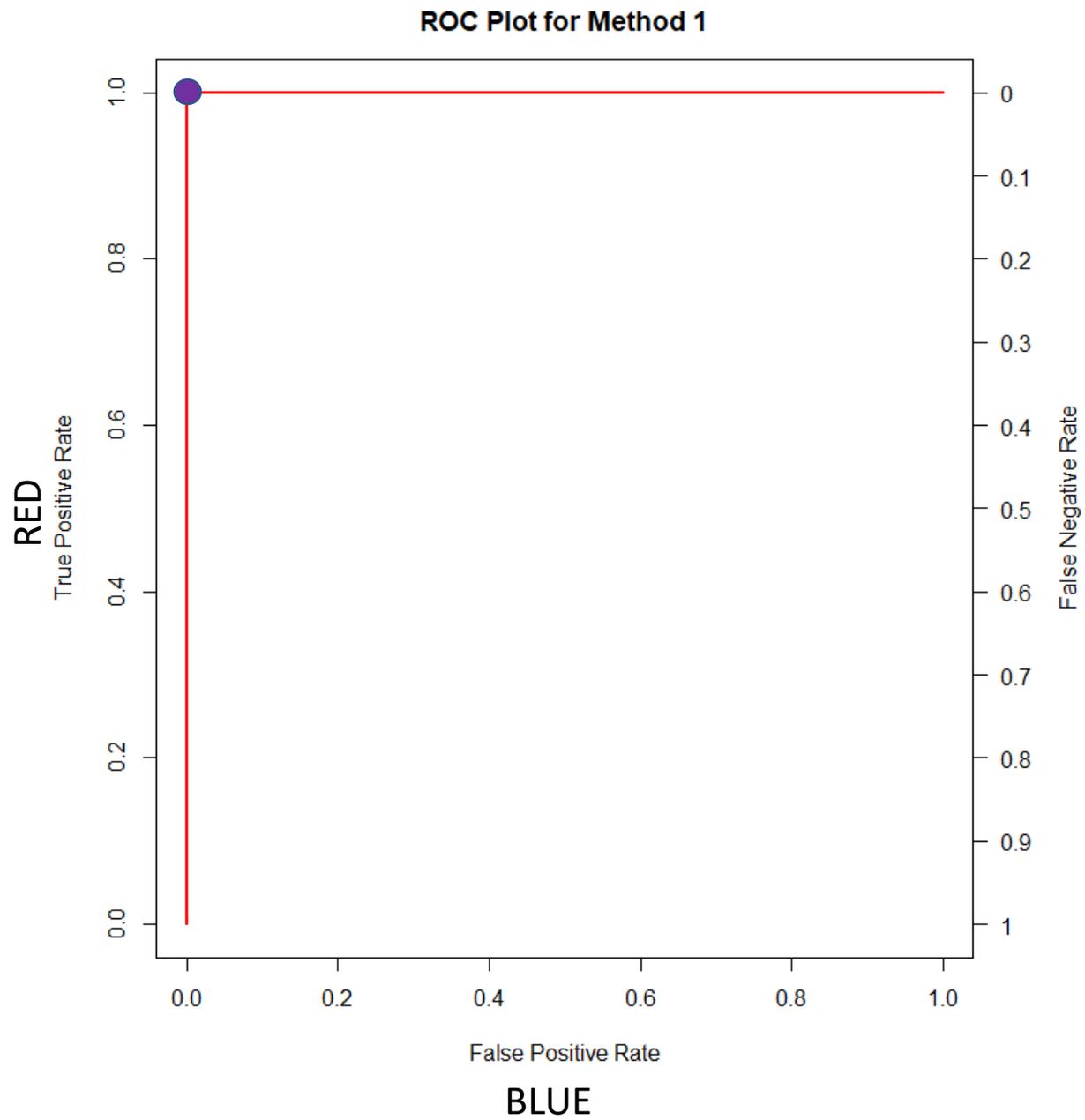
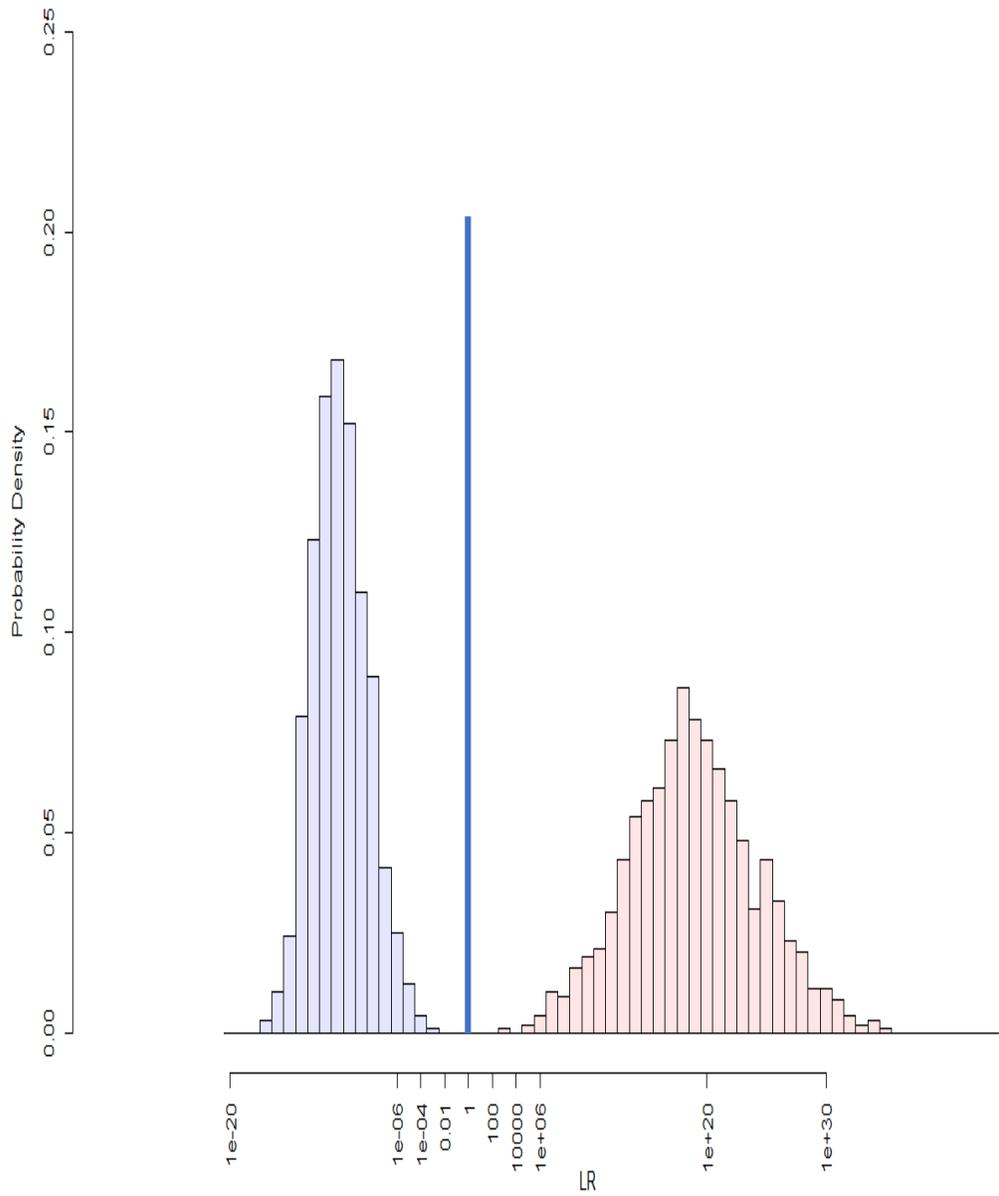


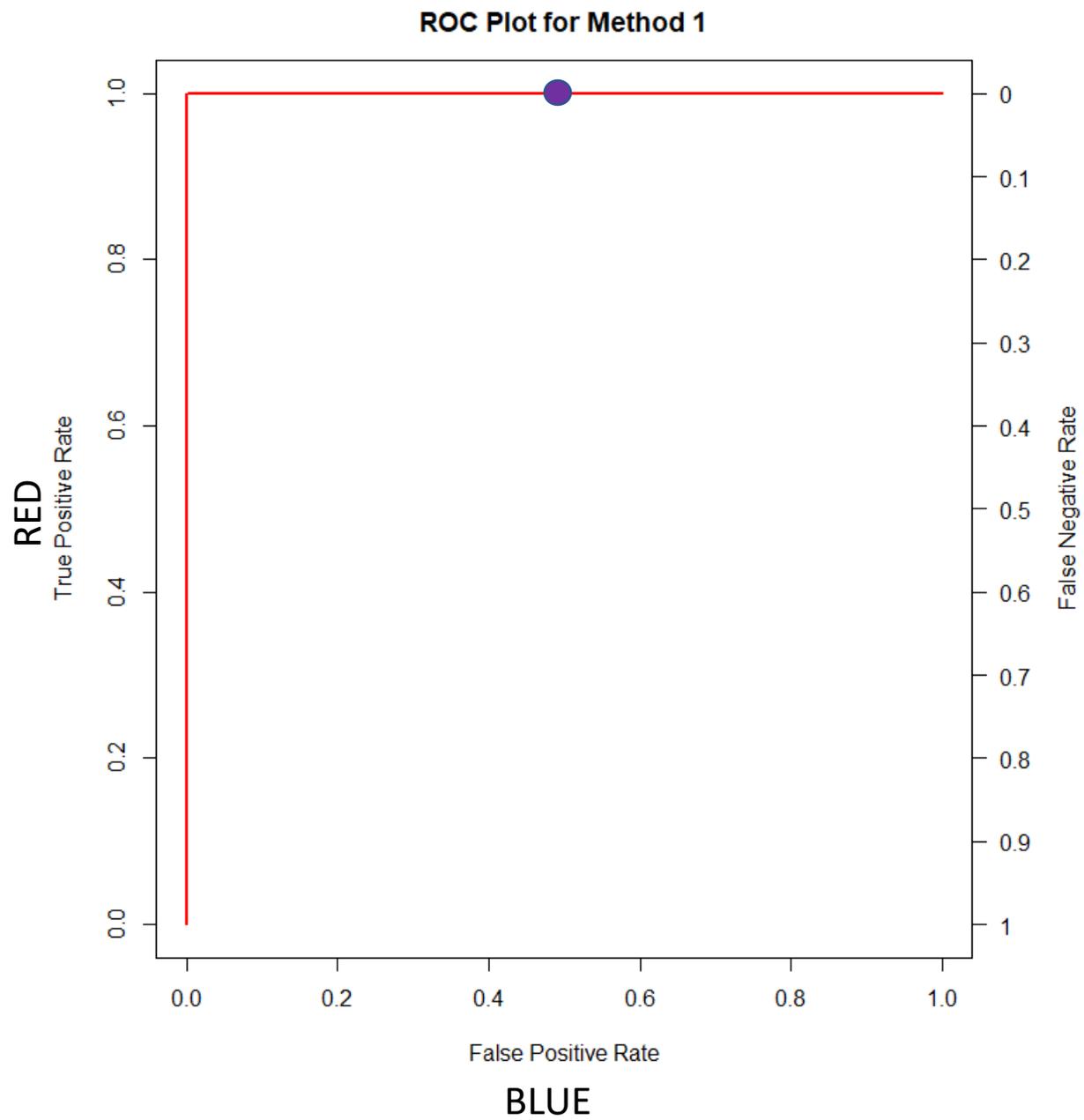
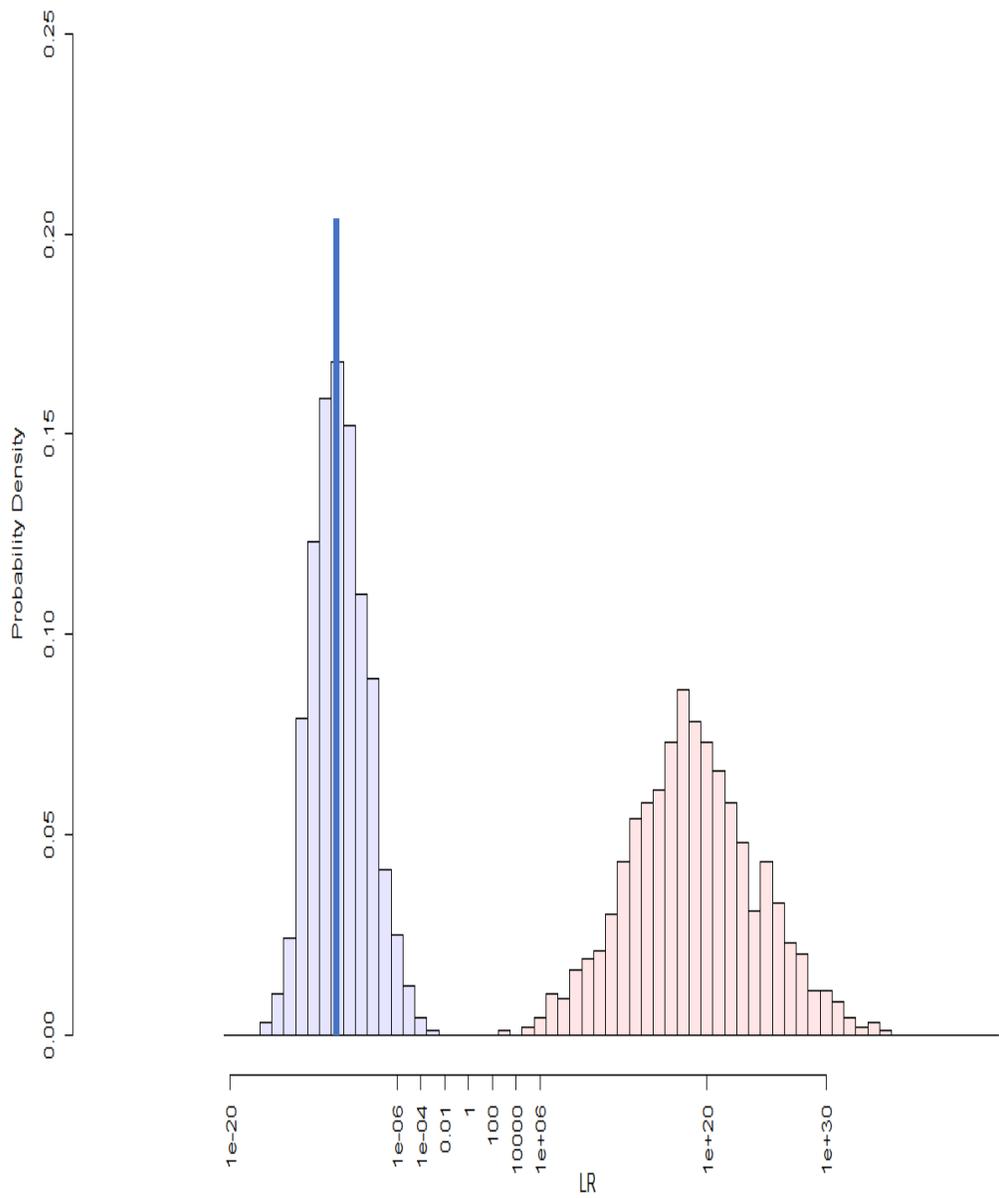


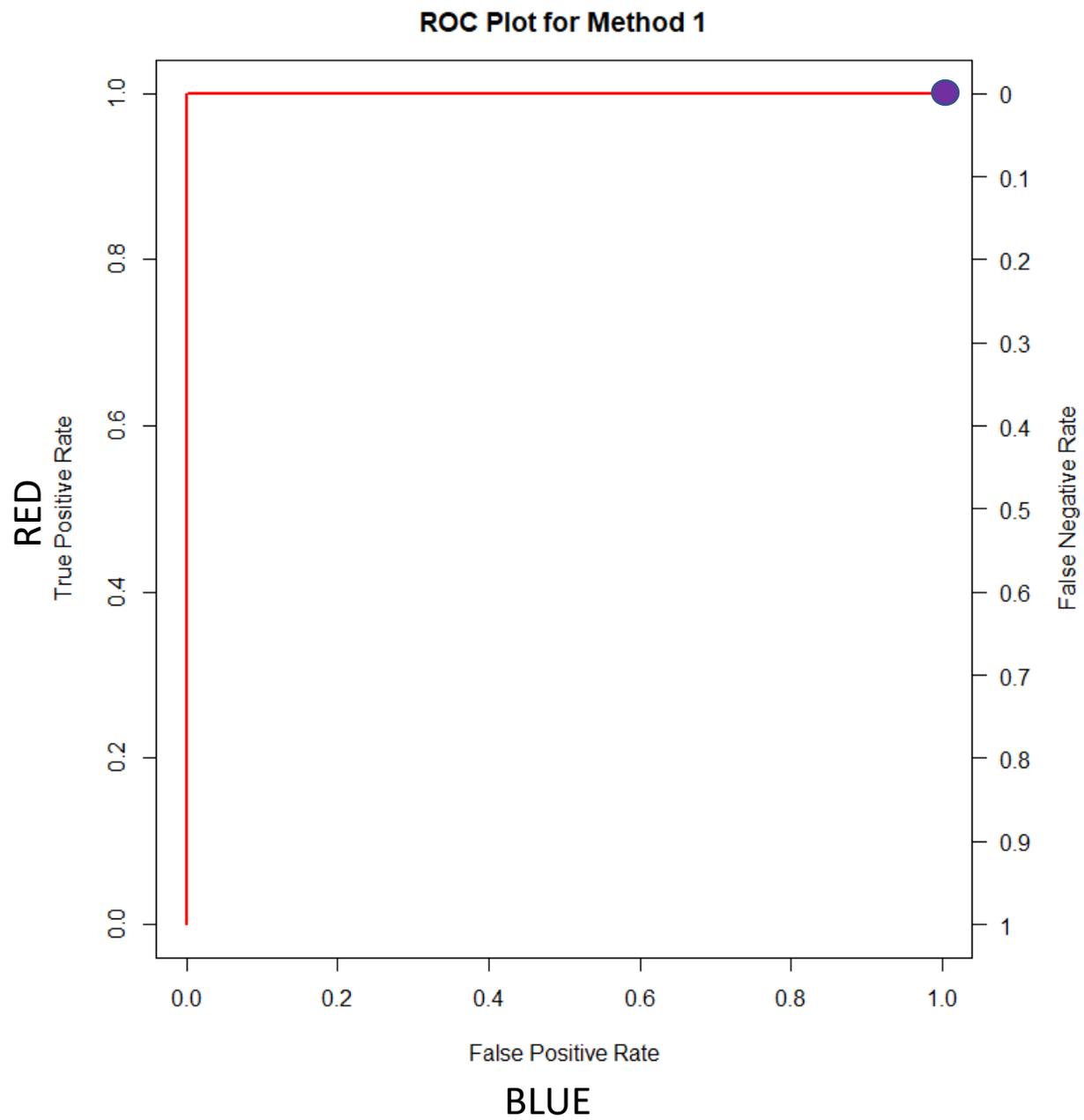
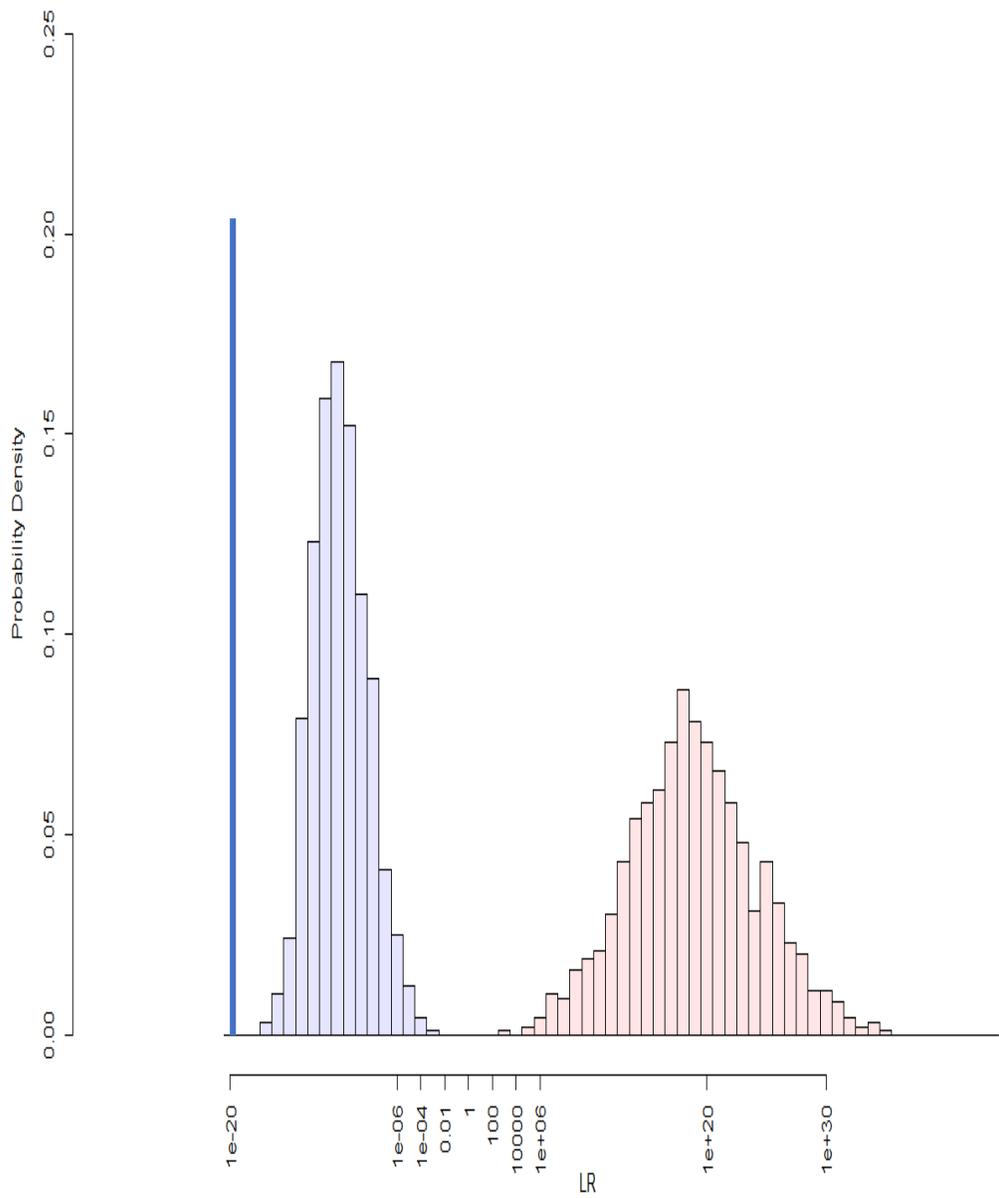
ROC = Receiver Operating Characteristic

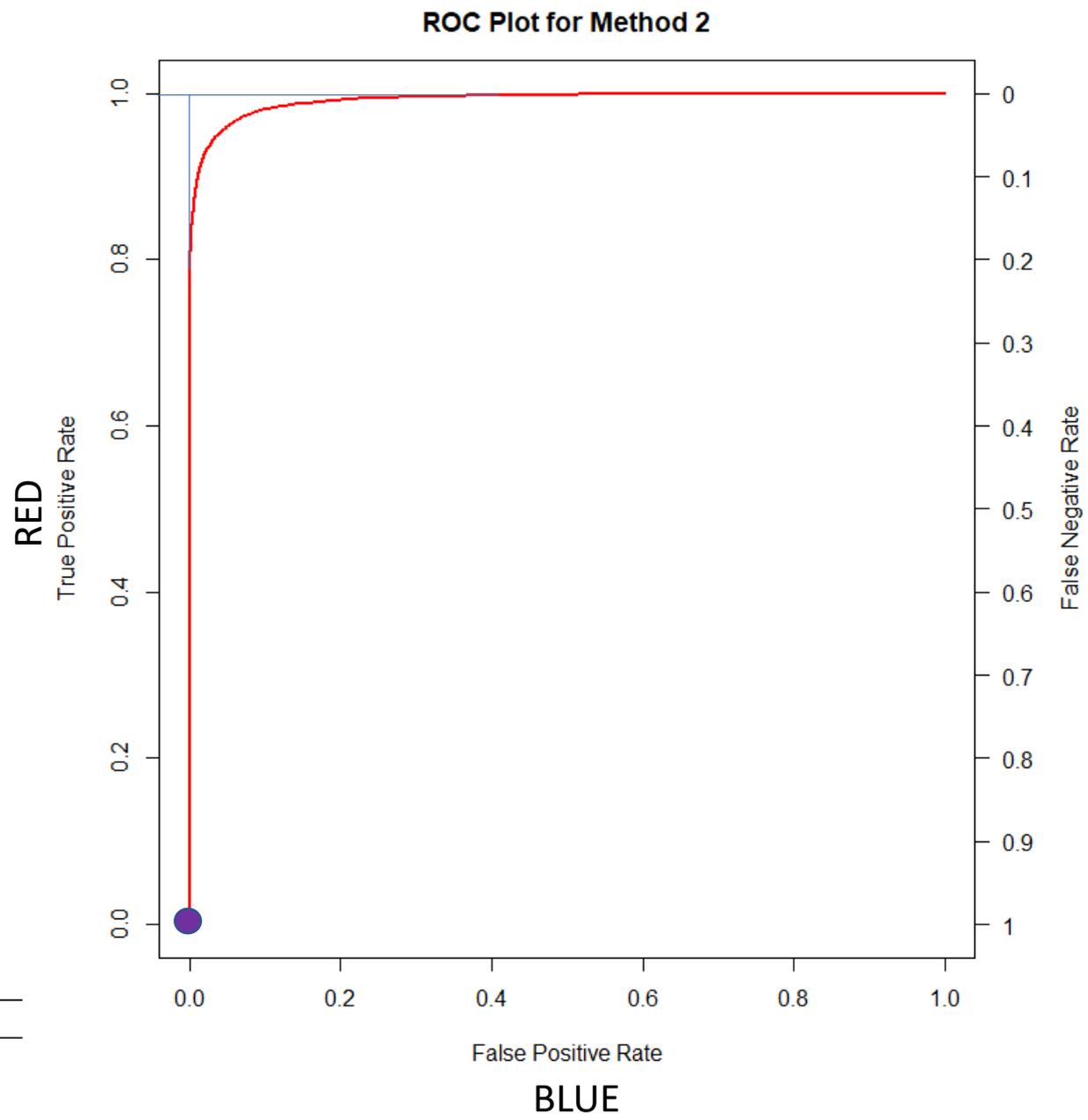
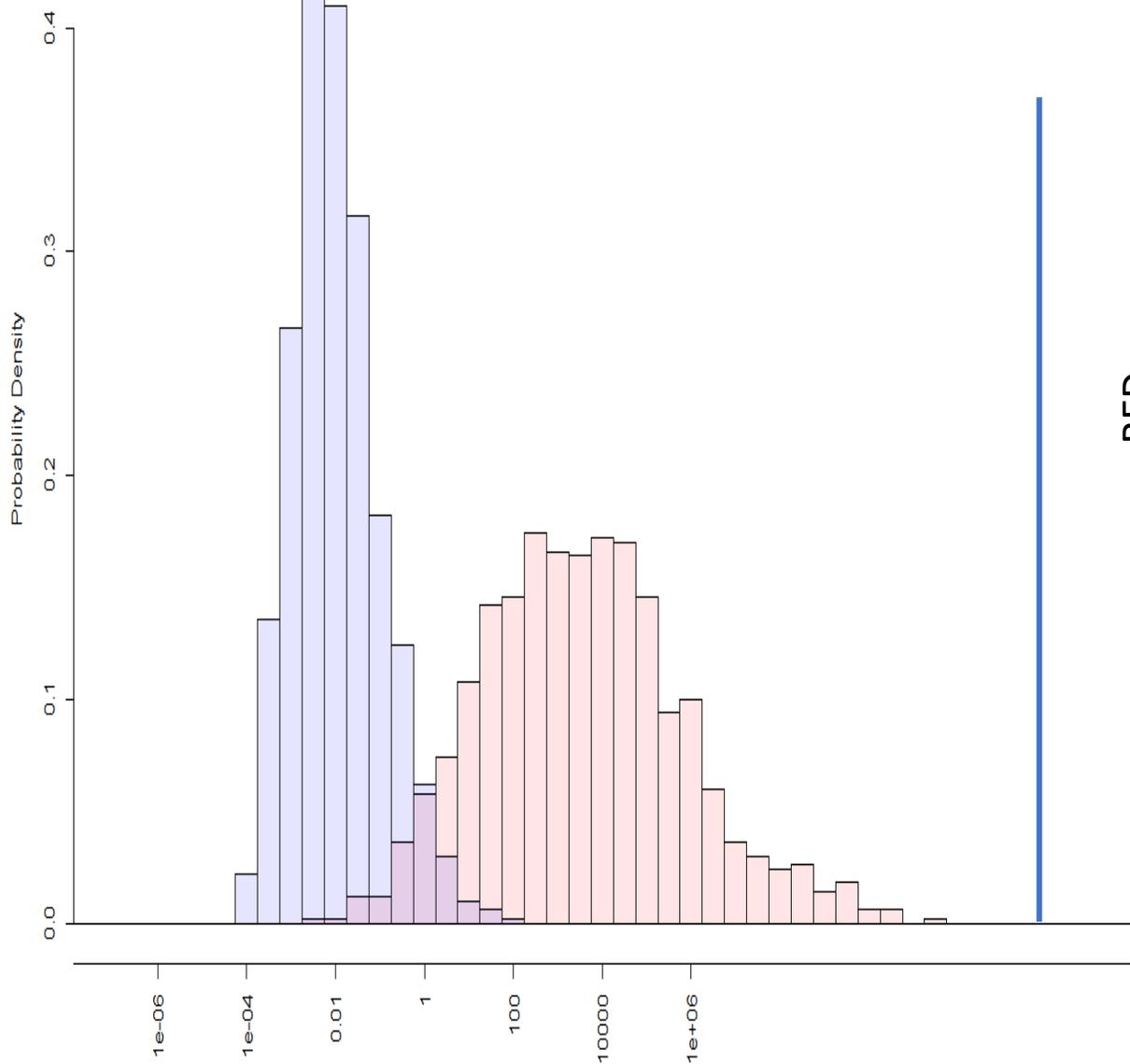


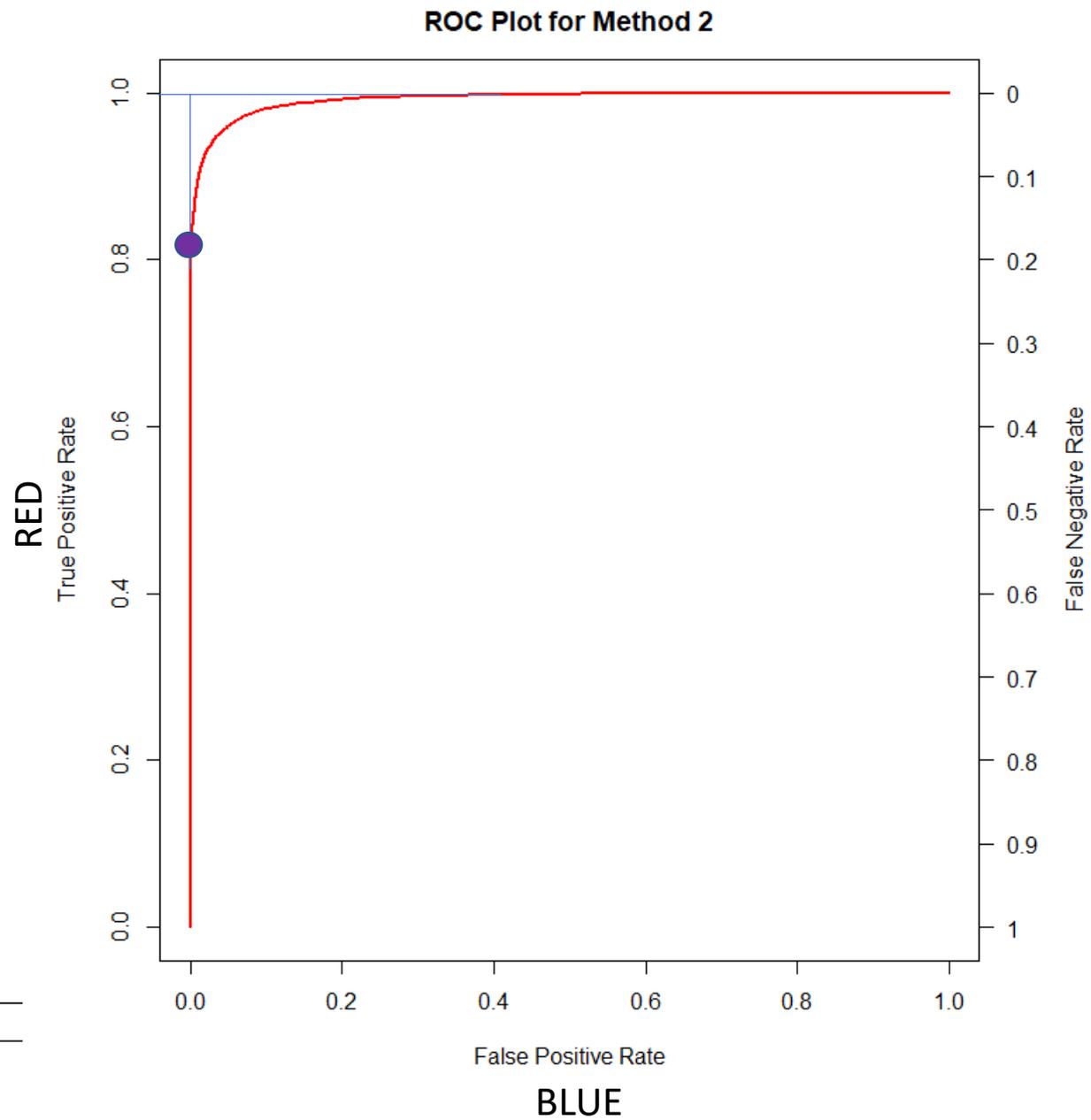
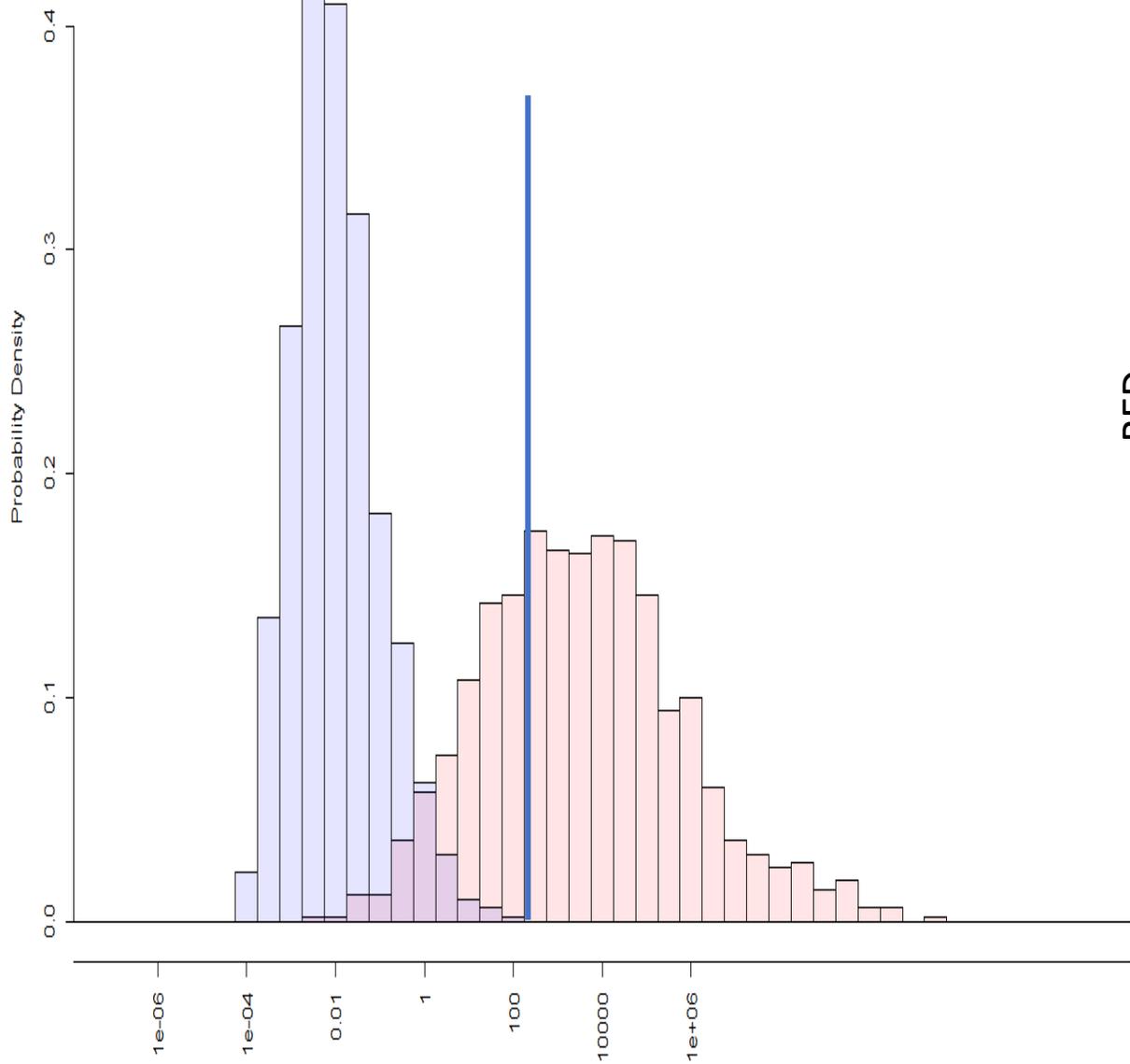


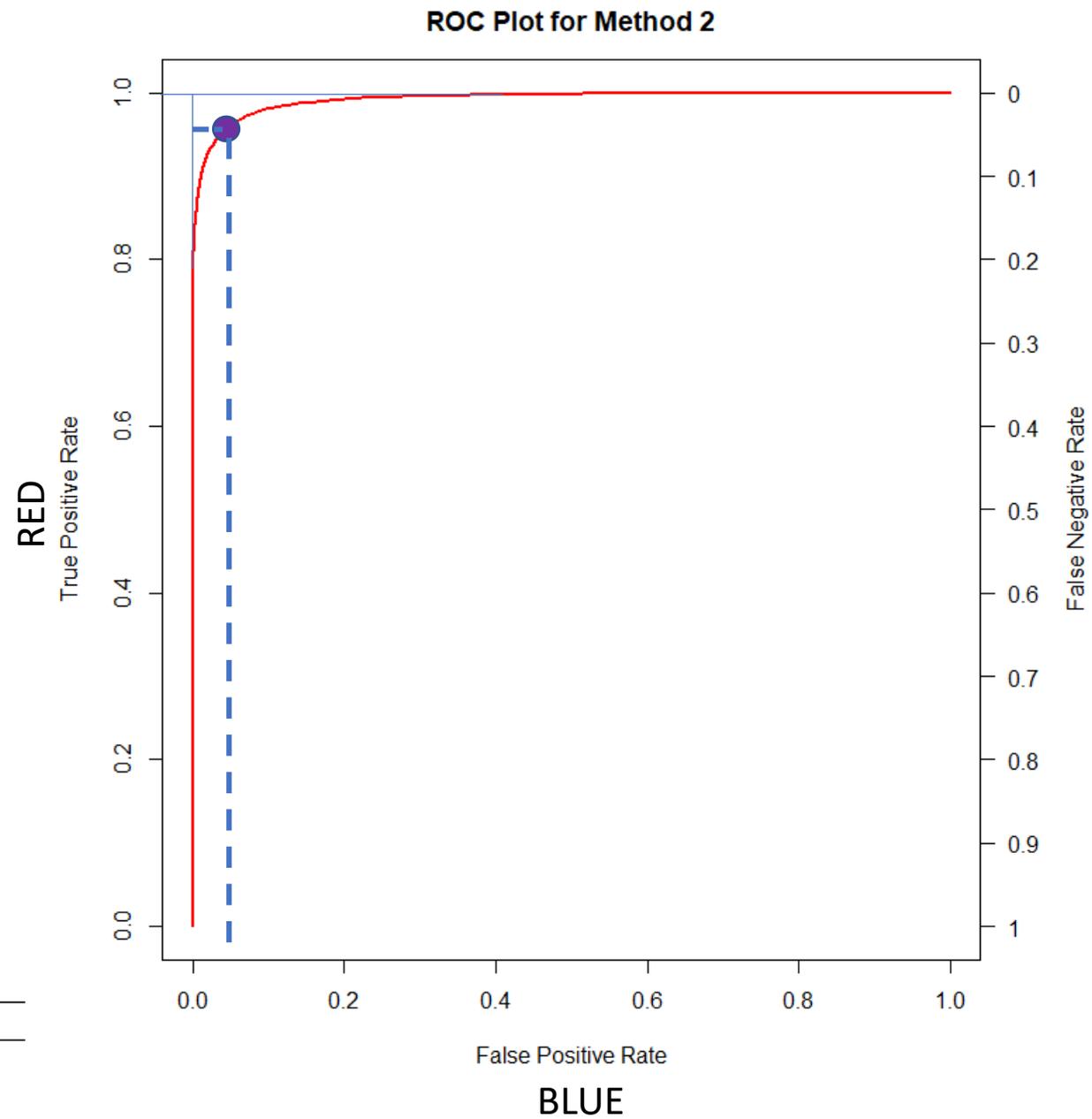
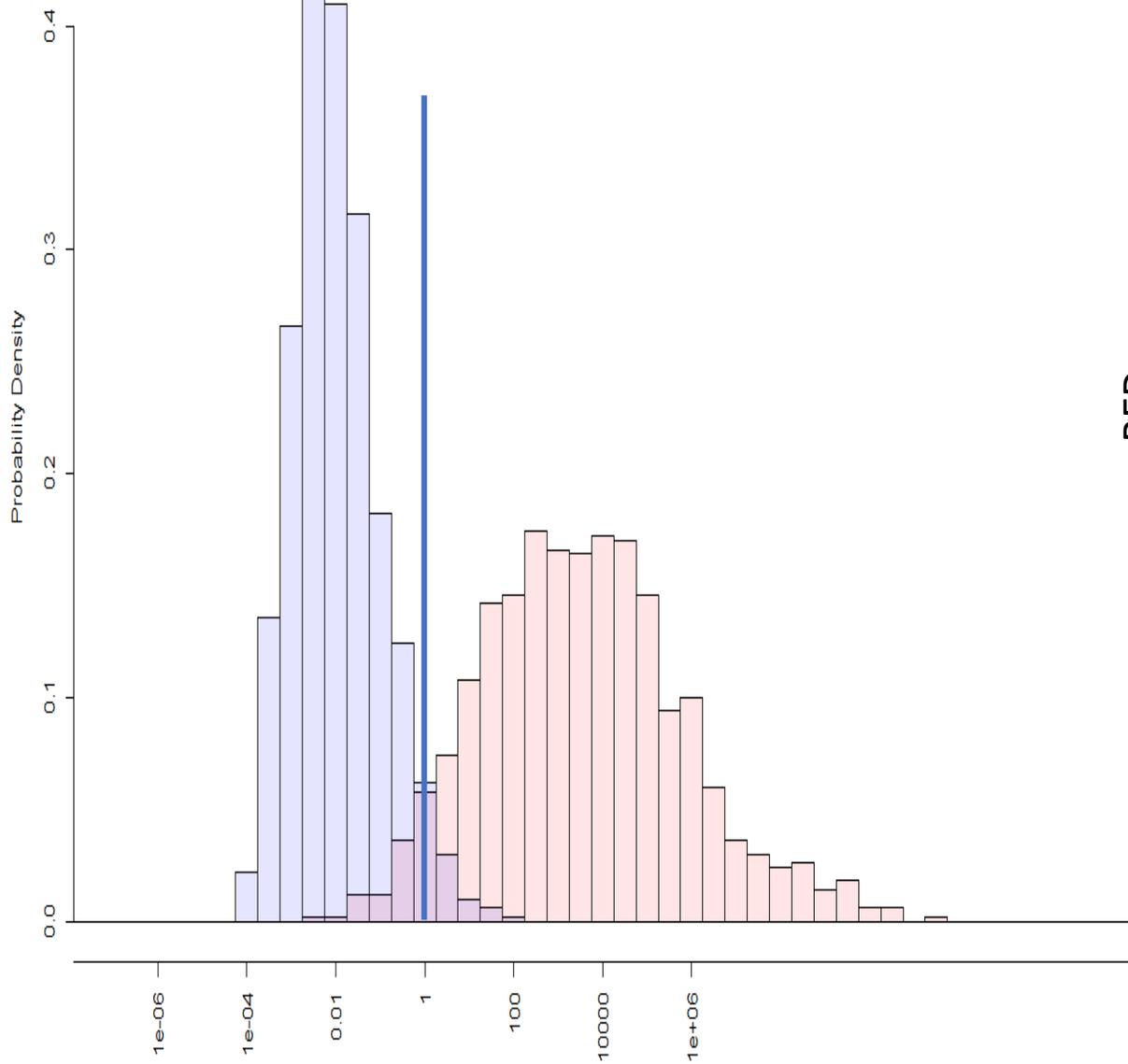


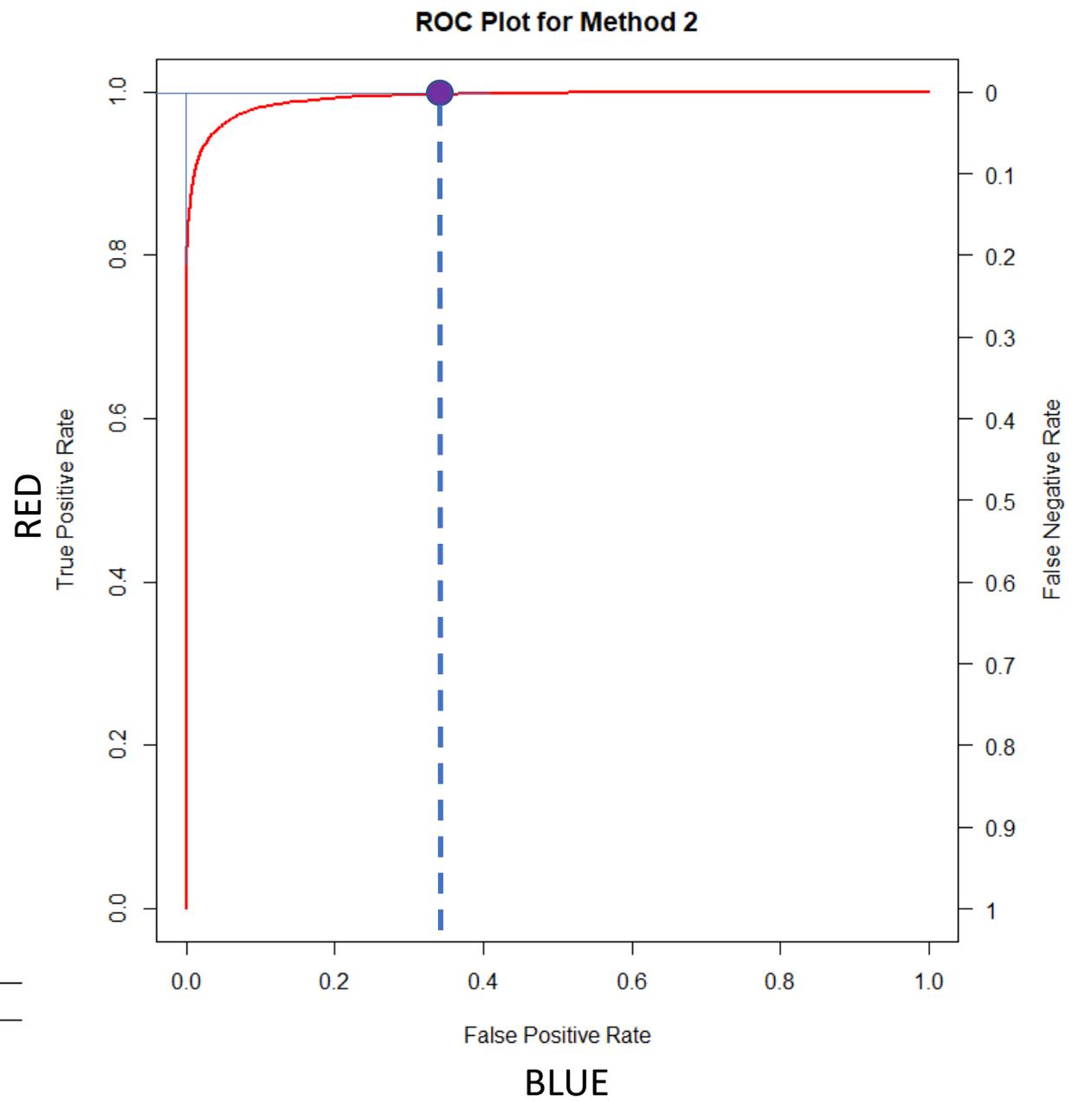
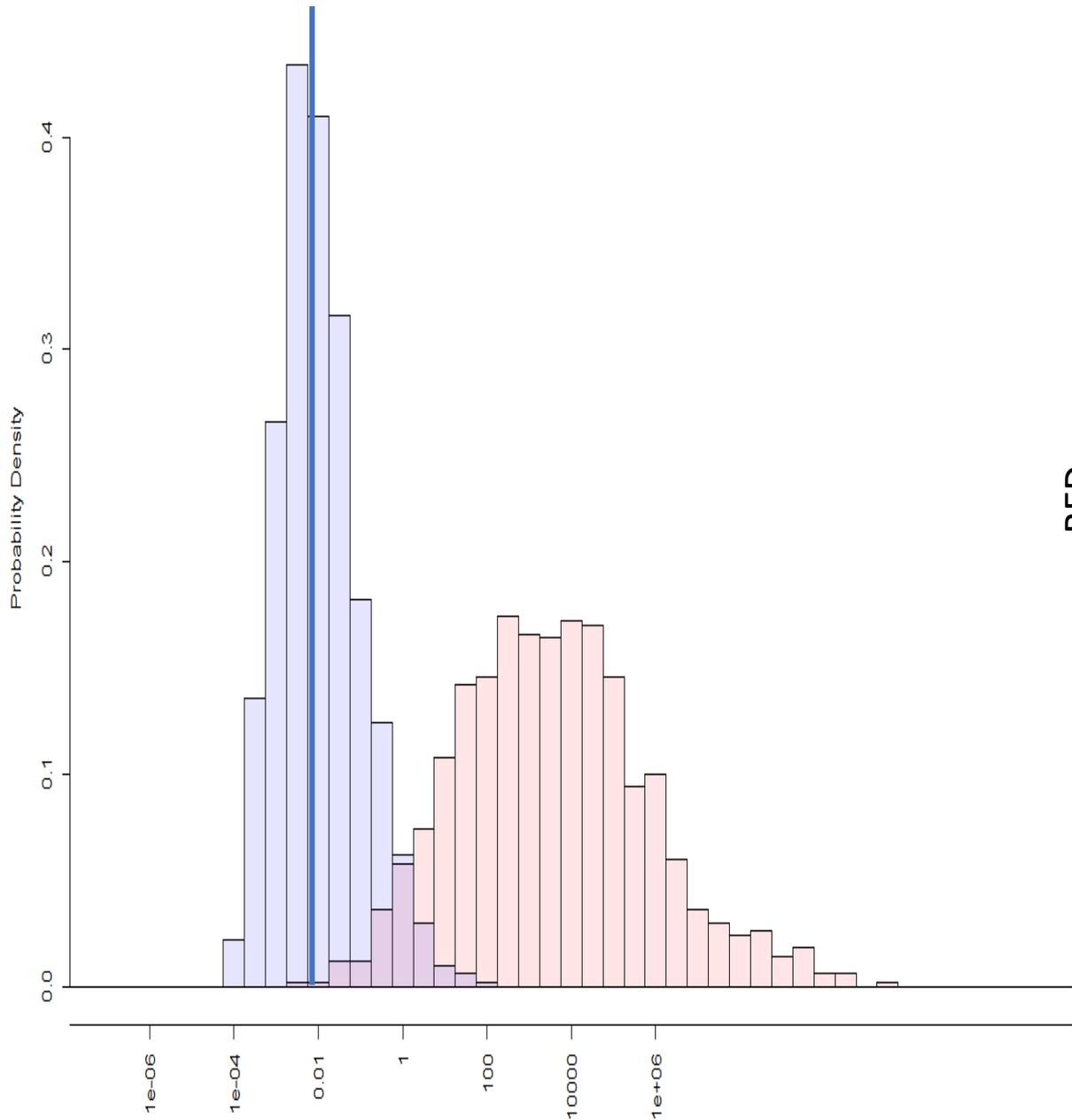


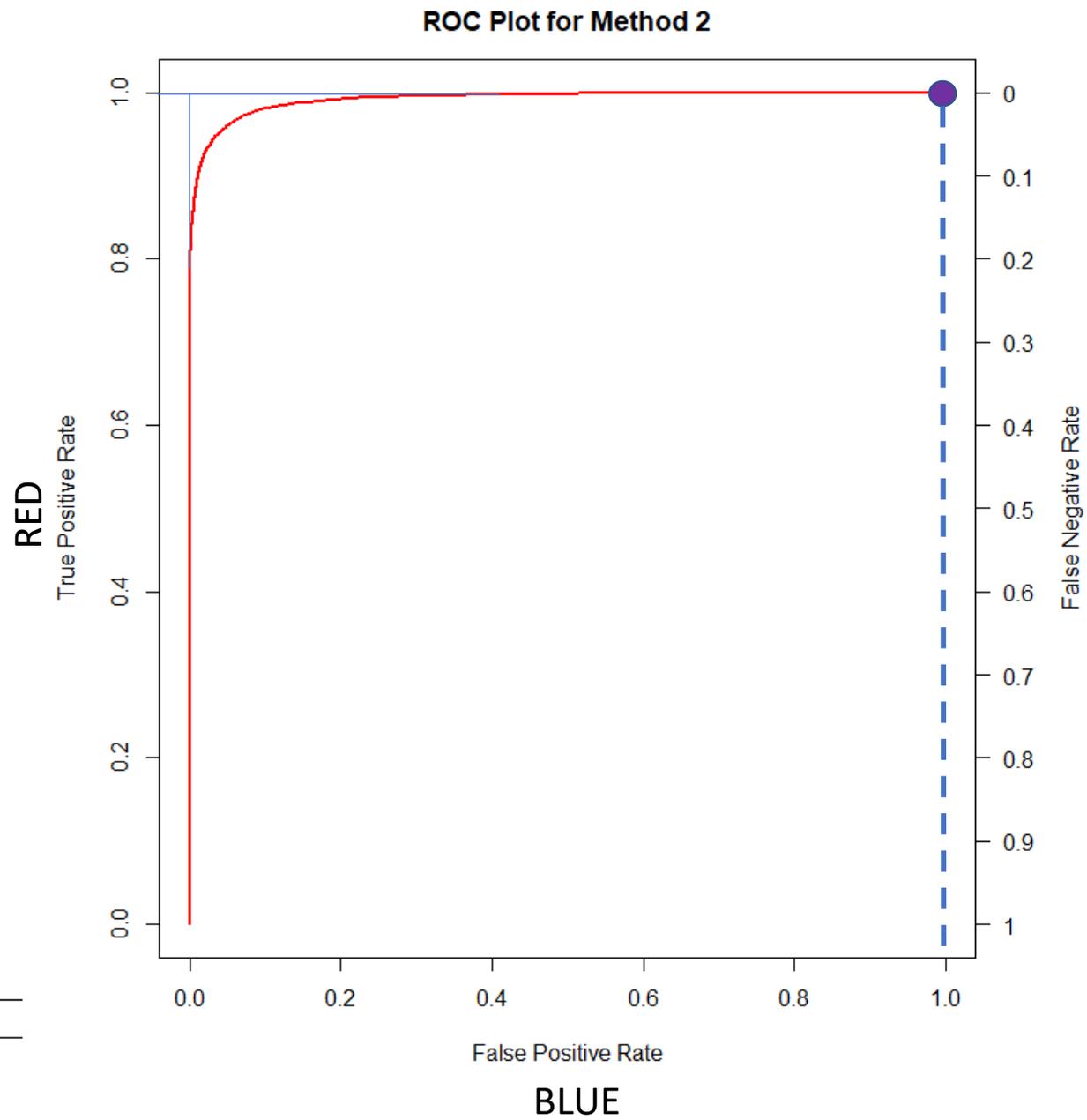
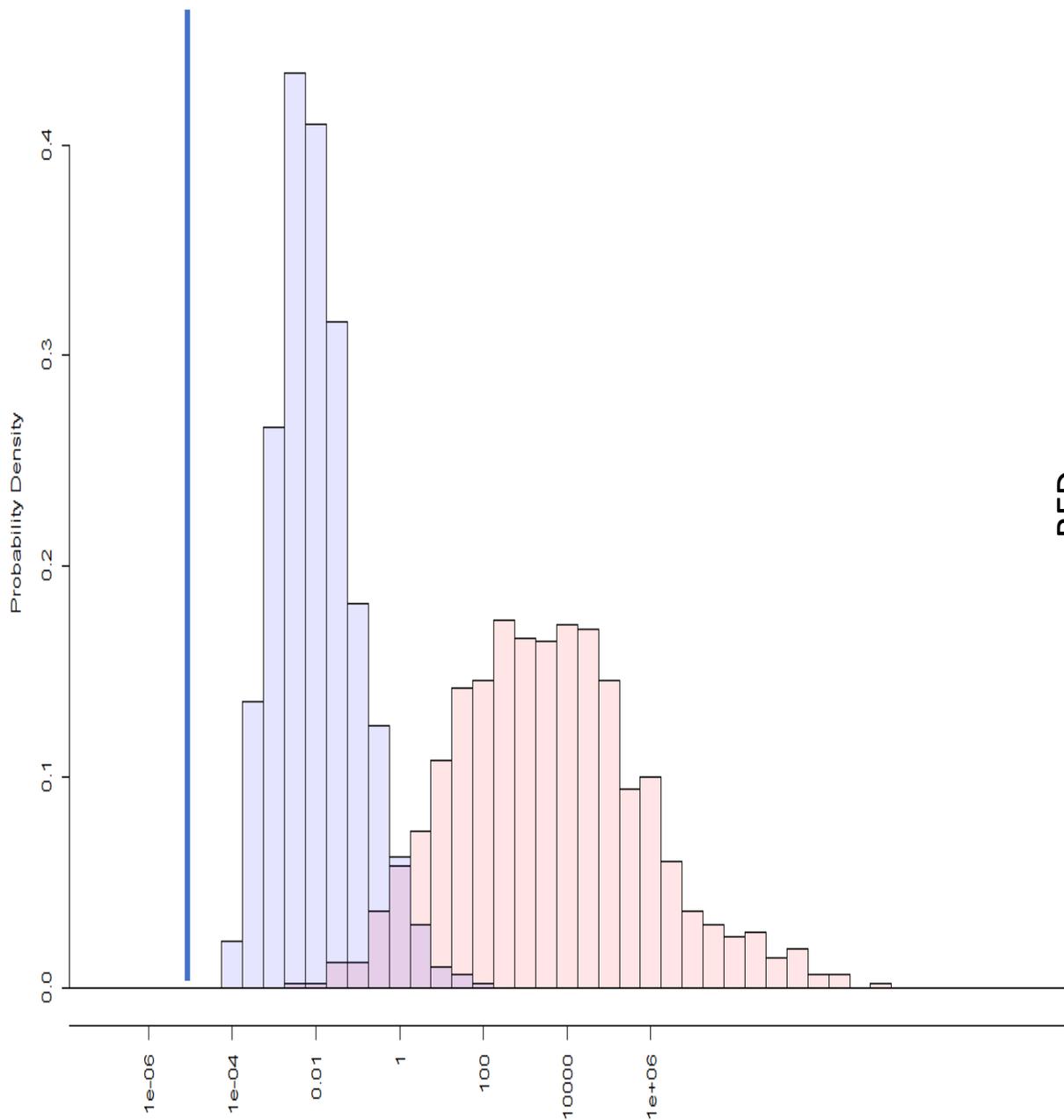


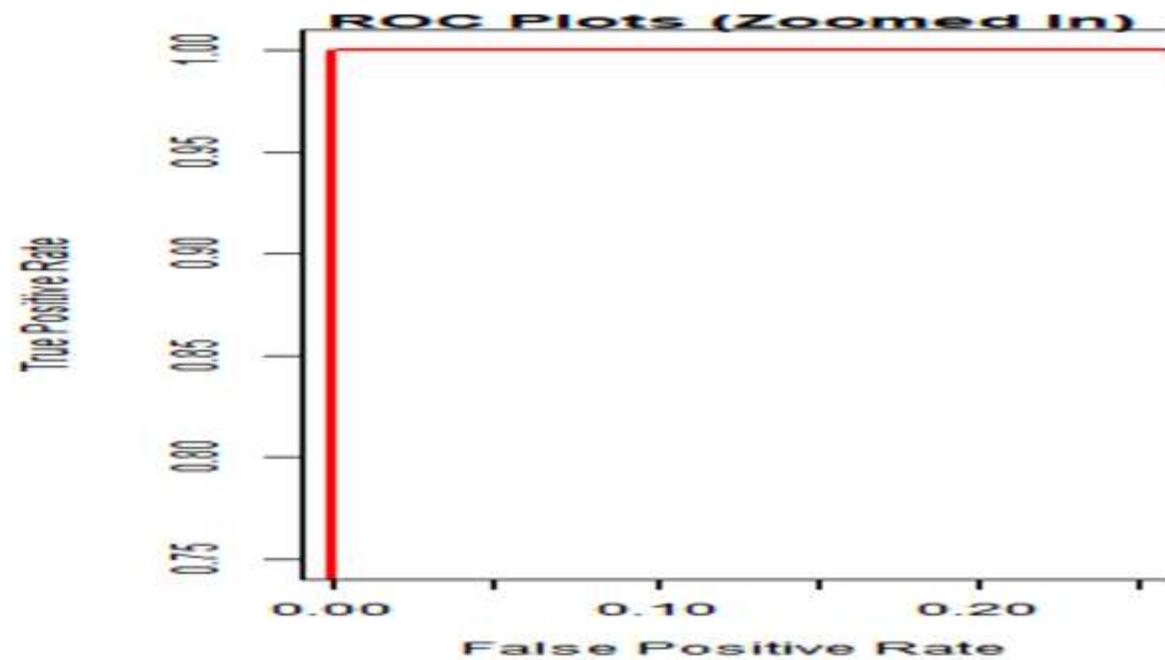
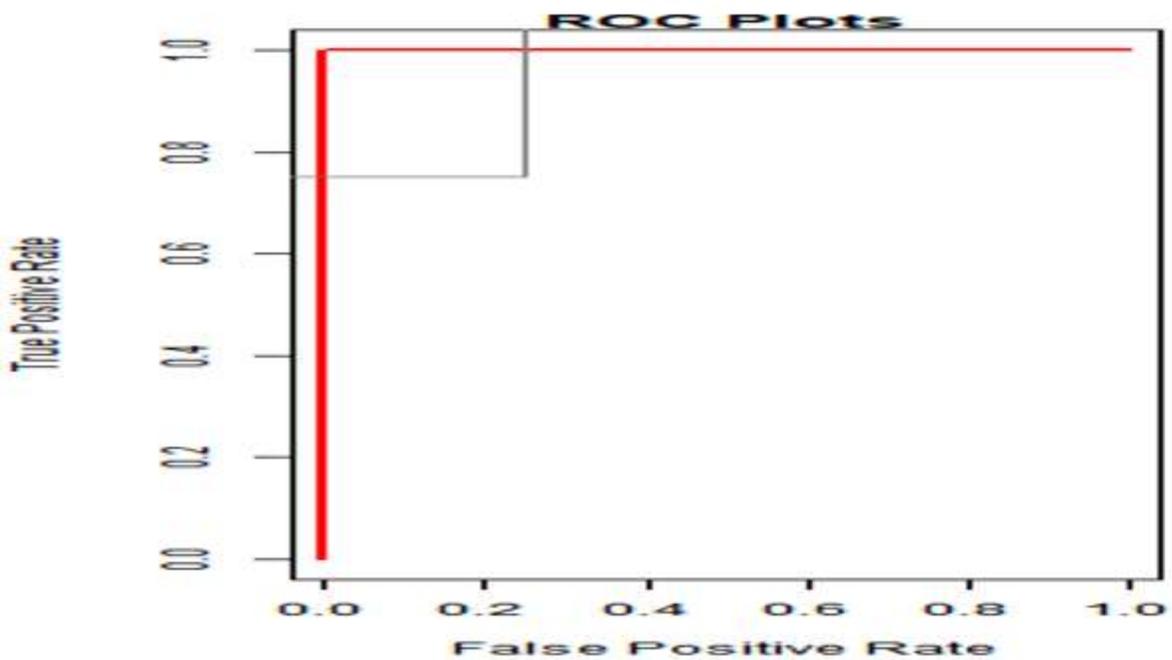
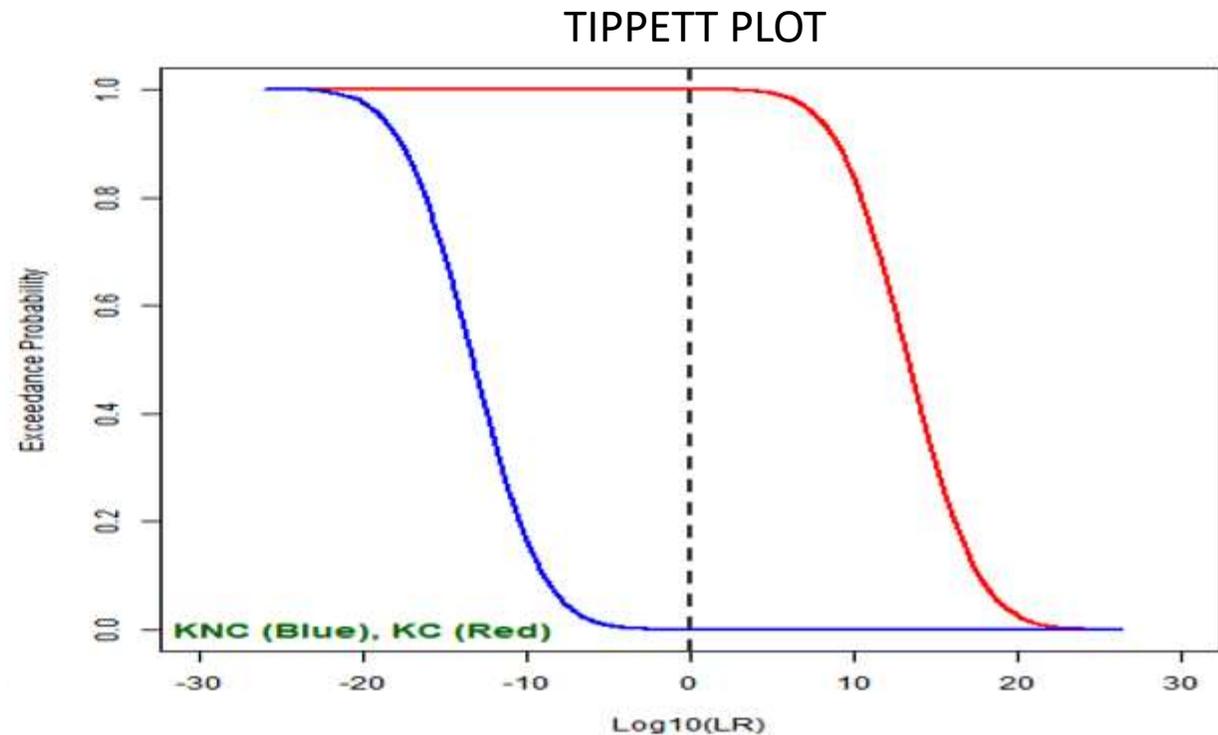
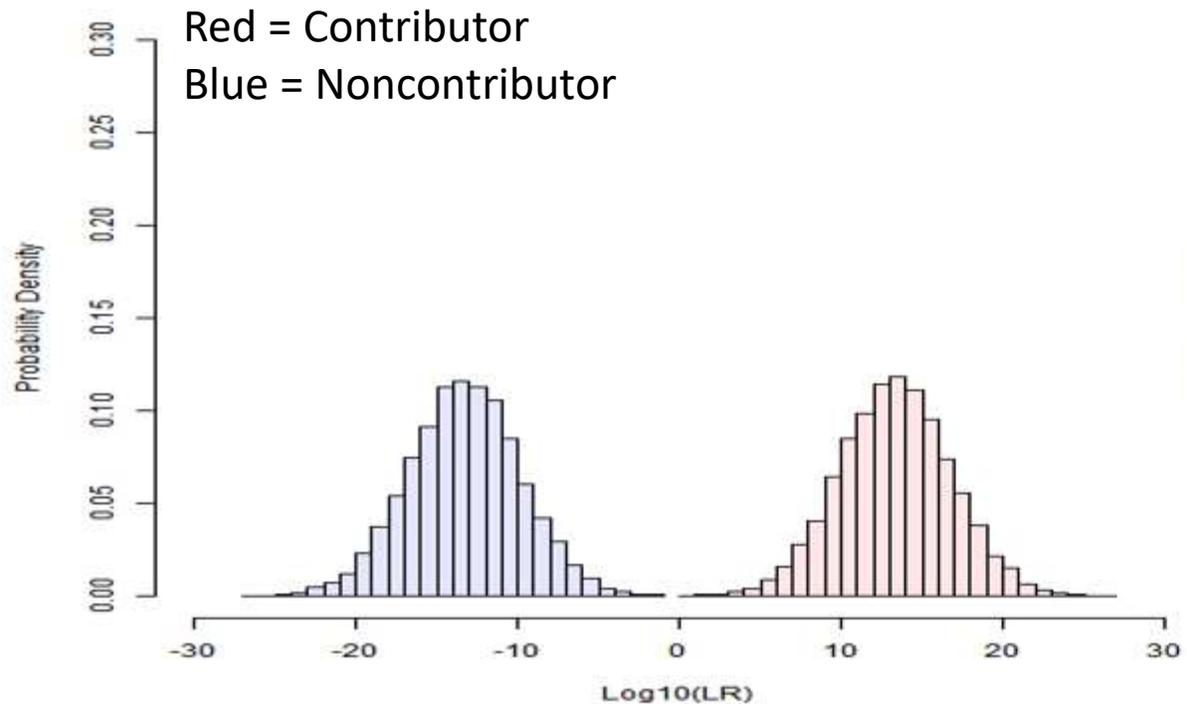


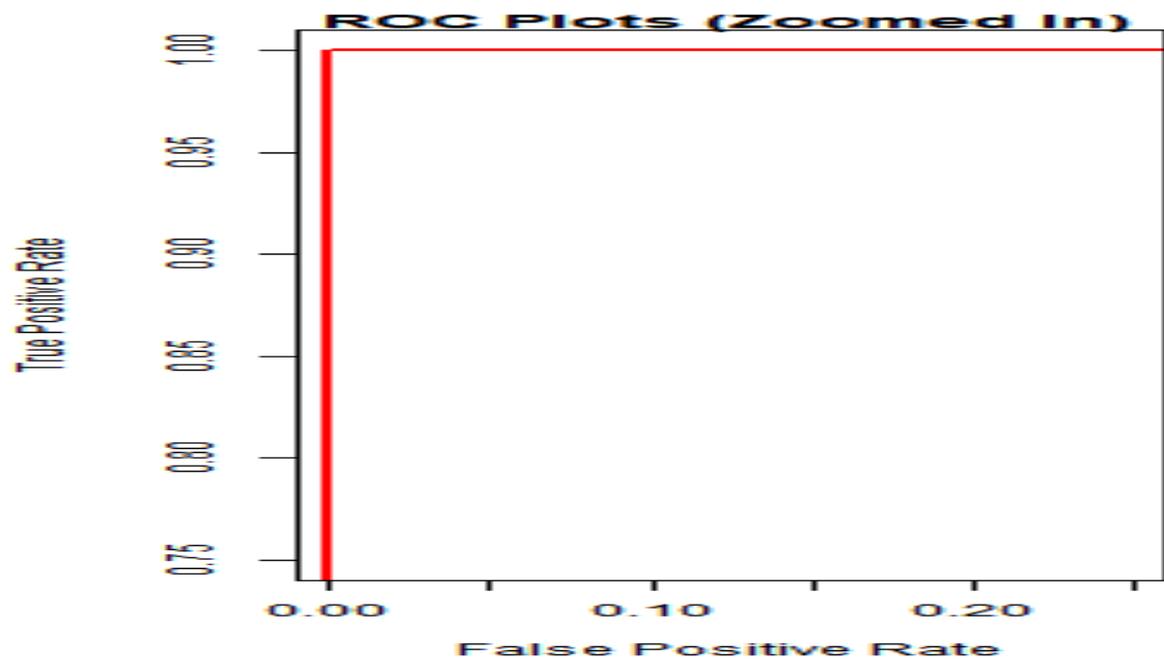
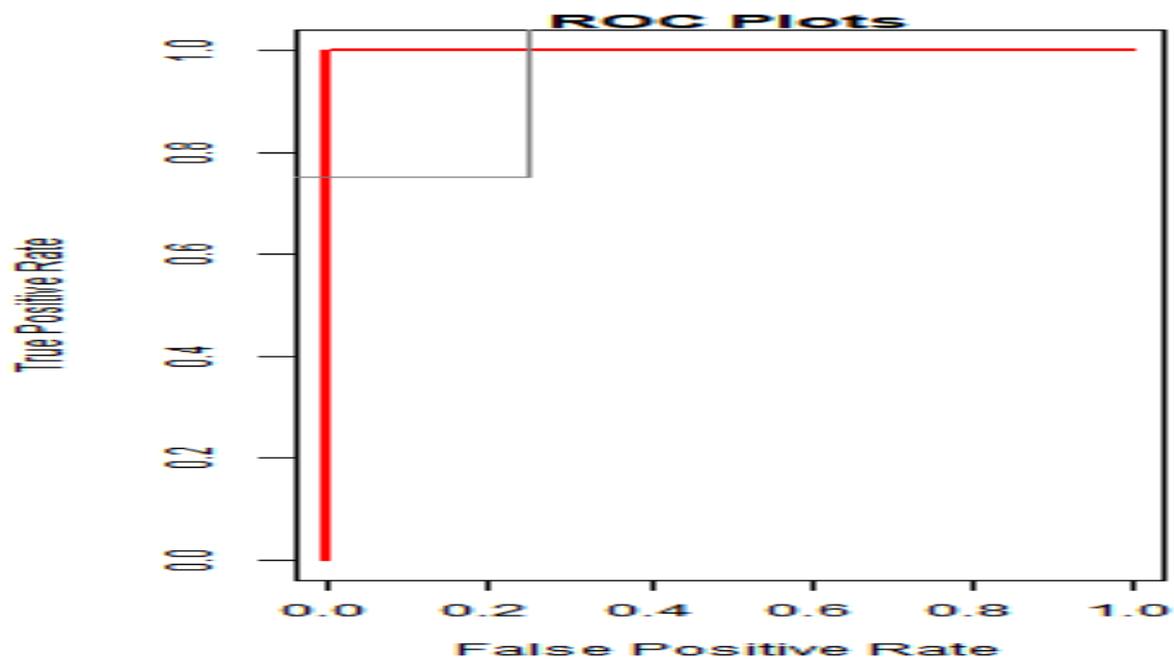
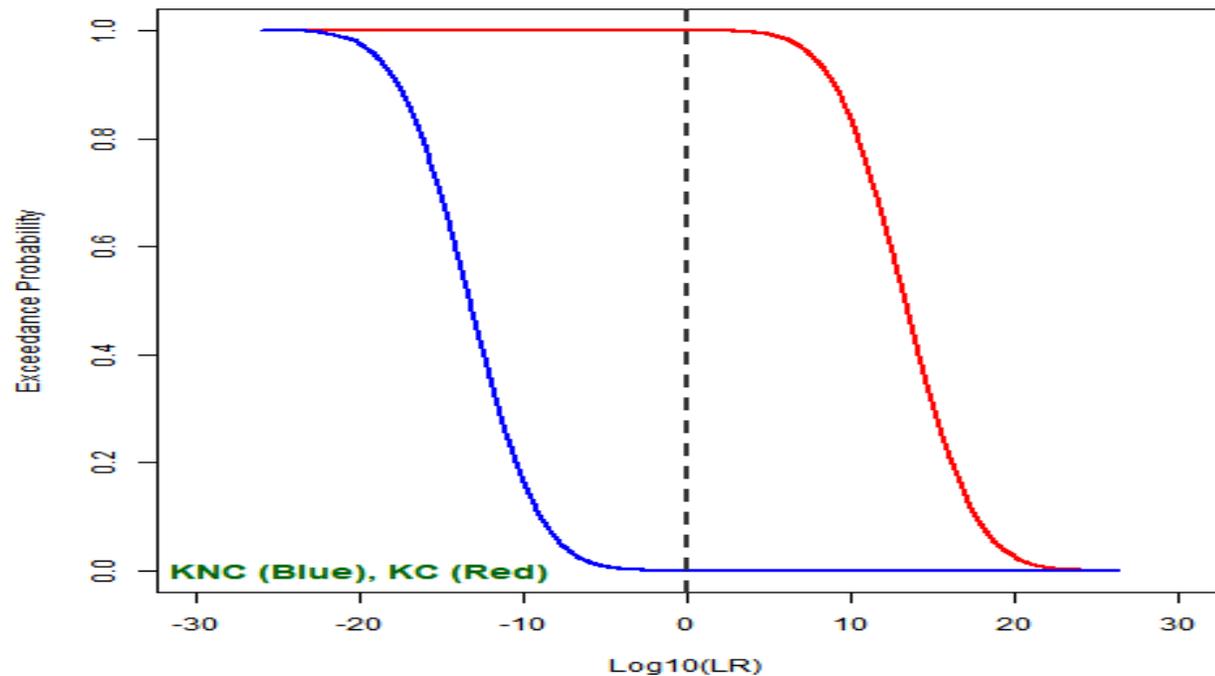
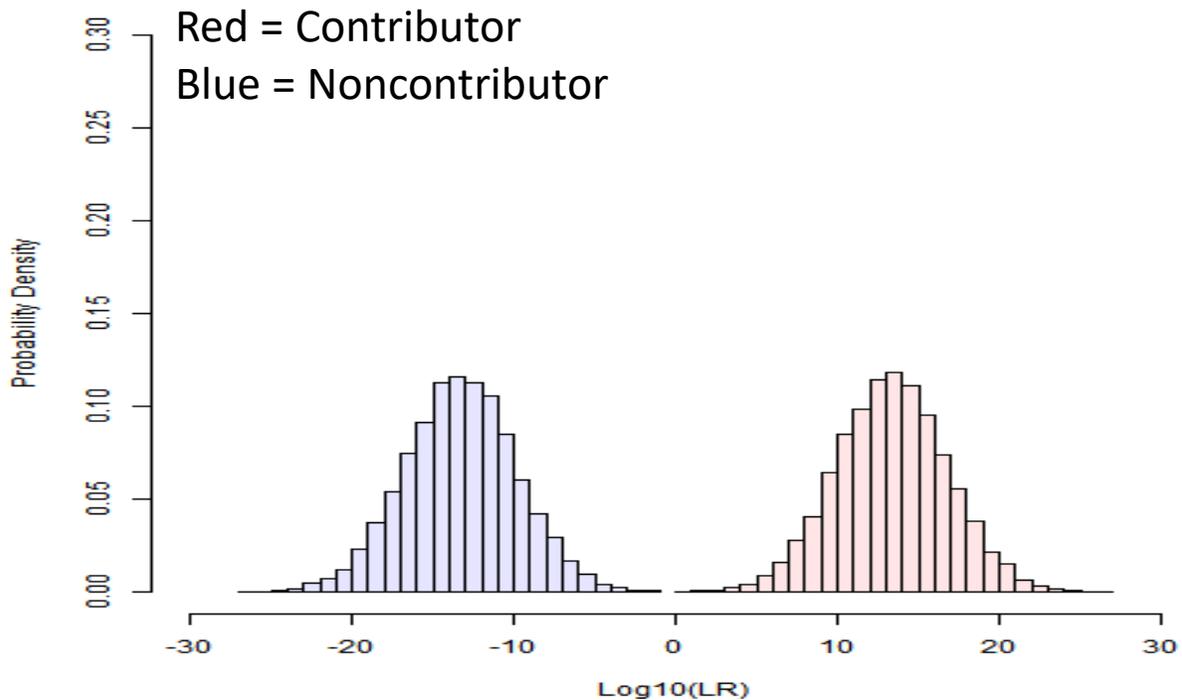












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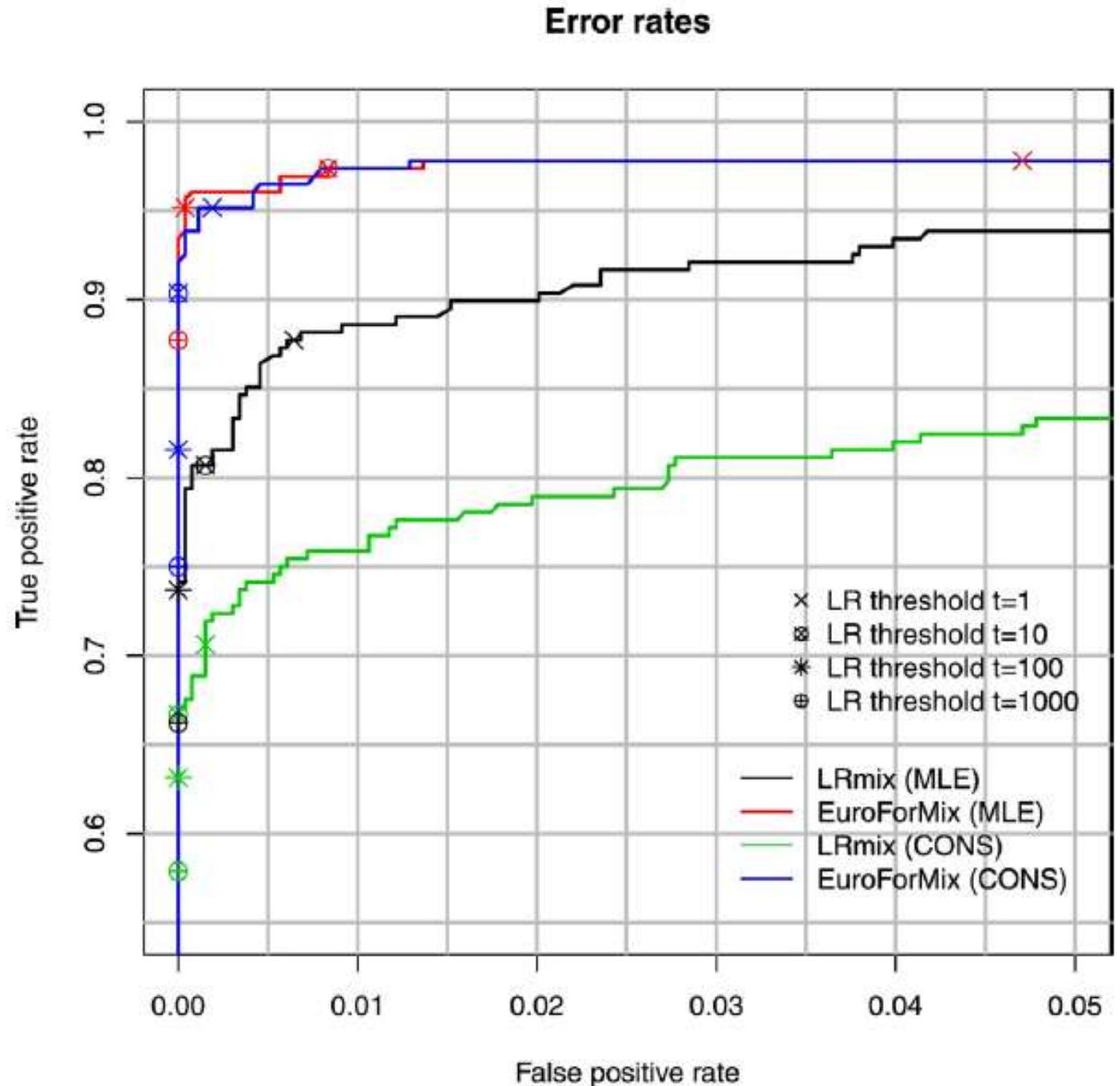
journal homepage: www.elsevier.com/locate/faig

Research paper

A comparative study of qualitative and quantitative models used to interpret complex STR DNA profiles

Øyvind Bleka^{a,b,*}, Corina C.G. Benschop^c, Geir Storvik^b, Peter Gill^{a,d}

Fig. 2. Receiver operating characteristic (ROC) plot where the rate of false positives (FP) (along horizontal axis) and true positives (TP) (along vertical axis) are plotted as a function of LR thresholds. The plot shows the results for the maximum likelihood estimation method (MLE) and the conservative method (CONS) for both LRmix and EuroForMix. The points on the curves show the FP and TP rates for different LR thresholds.



Some Take-aways

1. Primary focus should be on LR system reliability
 - Improvement in System Reliability can be accomplished by improving component reliabilities
 - Optimal strategies for this may focus on those components that affect system reliability the most. (Sensitivity analysis)

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The proof of the pudding is in the eating of it.



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3. When examining experimental results from reliability studies determine whether the experiment focused on selected parts of the system or on the entire system. Otherwise claims of reliability cannot be properly interpreted.
4. There is no single correct LR. **HOWEVER**, there are LR systems that perform sub-optimally relative to other LR systems.

Some Take-aways

5. One LR system may appear to be as reliable as another based on aggregate measures. However, a system can perform better than another in selected scenarios and vice versa.
6. Different LR systems, even those regarded as equally reliable, will disagree in any given casework situation. The magnitude of this disagreement is crucial information for triers of fact. The disagreement, in a given case, needs to be studied and reported.

Item 6 was a key point made in the paper “Likelihood Ratio as Weight of Forensic Evidence: A Closer Look” (2018). There were at least 3 rebuttal papers or letters to the editor. We believe that they did not address any of our main concerns.

Likelihood Ratio as Weight of Forensic Evidence: A Closer Look

Steven P. Lund and Hari Iyer

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Rapid Communication

A response to “Likelihood ratio as weight of evidence: A closer look” by Lund and Iyer

Simone Gittelson ^a  , Charles E.H. Berger ^b, Graham Jackson ^{c, d}, Ian W. Evett ^e, Christophe Champod ^f, Bernard Robertson ^g, James M. Curran ^h, Duncan Taylor ^{i, j}, Bruce S. Weir ^k, Michael D. Coble ^{l, m}, John S. Buckleton ^{k, n}



Commentary: Likelihood Ratio as Weight of Forensic Evidence: A Closer Look

Colin Aitken ^{1*}, Anders Nordgaard ², Franco Taroni ³ and Alex Biedermann ³

¹ School of Mathematics, University of Edinburgh, Edinburgh, United Kingdom, ² National Forensic Centre (Sweden), Linköping, Sweden, ³ School of Criminal Justice, Université de Lausanne, Lausanne, Switzerland

Keywords: likelihood ratio, value of evidence, forensic science, logarithm, forensic reporting



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Reliability Studies

- Is the study focusing on one specific component of the system?
- Is the study addressing end-to-end (system) reliability?
- How were the test samples (ground truth known) selected?
- How many independent subject profiles were considered?
- Were the H_d true profiles synthetically generated OR were they obtained from a random sample of subjects?
- Does the conclusion state that “a process is **reliable**” or is it giving **measures of reliability**?

QUESTIONS ?